UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION	
This document relates to:	MDL No. 2804
The County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al., Case No. 18-op-45090	Hon. Dan Aaron Polster
The County of Cuyahoga, Ohio, et al. v. Purdue Pharma L.P., et al., Case No. 17-op-45004	

Expert Report of Gregory K. Bell, Ph.D.

May 10, 2019

Table of Contents

I. INTRODUCTION

A. Qualifications

1. I am a Group Vice President at Charles River Associates ("CRA"), an economics and management consulting firm. My education includes an M.B.A. and a Ph.D. in business economics, both from Harvard University, and a B.A. from Simon Fraser University. Details of my professional experience, publications, and past testimony are described in my curriculum vitae, a copy of which is attached as Exhibit I-1. CRA receives compensation for my time at a rate of $850 per hour. Neither CRA's nor my compensation depends on the content of my opinions or on the outcome of this litigation.

2. For the past twenty-six years, I have led CRA's Life Sciences practice, which focuses on economic issues in the pharmaceutical, biotechnology, medical device, and diagnostic industries. In this capacity, I have led many projects concerning business economics in the life sciences industries. Much of this work has focused on lifecycle analytics and management, addressing strategic challenges for therapeutic agents or devices from commercial launch through replacement or generic competition, including with respect to pricing, payer and physician behavior, and competitive analysis in the U.S. and globally. With respect to pharmaceuticals indicated for the treatment of pain, I have led the pricing and managed care strategy to support the launches of products and led the competitive strategy analysis for a product about to face generic competition. In addition, I led the managed care strategy to support the launch of a product indicated for the treatment of opioid addiction.

3. As noted in Exhibit I-1, I have submitted numerous expert reports and given testimony before many courts and arbitrators in North America, Europe, and Asia involving issues in the life sciences industries, including patent disputes, licensing, antitrust, valuation, and other concerns. With respect to pharmaceuticals indicated for the treatment of pain, I have provided expert

witness reports and testimony regarding commercial success, market definition, access, and damages. In addition, I have testified on commercial success regarding a product indicated for the treatment of opioid addiction.

B. Assignment

4. In complaints filed in these actions[1] and consolidated in Multi-District Litigation No. 2804, The County of Summit, Ohio, et al. ("Summit"); and The County of Cuyahoga, Ohio, et al. ("Cuyahoga"; together, the "Counties") "assert two categories of claims: claims against the pharmaceutical manufacturers of prescription opioid drugs that engaged in a massive false marketing campaign to drastically expand the market for such drugs and their own market share, and claims against entities in the supply chain that reaped enormous financial rewards by refusing to monitor and restrict the improper distribution of these drugs."[2]

5. Among the "entities in the supply chain" are defendants AmerisourceBergen Drug Corporation ("ABDC"); Cardinal Health, Inc. ("Cardinal"); HBC Service Company ("HBC"); McKesson Corporation ("McKesson"); H. D. Smith, LLC f/k/a H. D. Smith Wholesale Drug Company ("H.D. Smith"); Rite Aid of Maryland, Inc., d/b/a Mid-Atlantic Customer Support Center ("Rite Aid"); and Walgreens Boots Alliance, Inc. ("Walgreens"; collectively, "Distributors").[3] With respect to Distributors, Plaintiffs allege: "The failure of the Defendants to maintain effective controls, and to investigate, report, and take steps to halt orders

---

1 In re National Prescription Opiate Litigation, United States District Court for the Northern District of Ohio, Eastern Division, Case No. 17-md-2804, Corrected Second Amended Complaint and Jury Demand, May 18, 2018 ("Summit Complaint"); In re National Prescription Opiate Litigation, United States District Court for the Northern District of Ohio, Eastern Division, Case No. 17-md-2804, Second Amended Corrected Complaint and Demand for Jury Trial, May 25, 2018 ("Cuyahoga Complaint"; collectively, "Complaints"). I am aware that Summit filed a Third Amended Complaint and Jury Demand on March 21, 2019; however, the Summit Complaint was in effect during the preparation of this report.

2 See Summit Complaint, ¶ 1; the language in the Cuyahoga Complaint is essentially identical (Cuyahoga Complaint, ¶ 1). Where appropriate, I refer to these two categories of entities collectively as "Defendants".

3 I note that the Complaints list other distributors of prescription drugs in defining the Distributor Defendants. Additionally, HBC, Rite Aid, and Walgreens are defined in at least one of the Complaints as "National Retail Pharmacies". See e.g., Summit Complaint, ¶ 127; Cuyahoga Complaint, ¶ 95.

that they knew or should have known were suspicious breached both their statutory and common law duties."[4] Plaintiffs further allege that Distributors' failure to report suspicious orders or otherwise to prevent diversion of prescription opioids caused an increase in overdose deaths and other adverse health and social consequences, which in turn allegedly caused the Counties to expend funds to respond to or alleviate those consequences through various departments.[5]

6. In connection with these claims, Plaintiffs have tendered a number of expert reports, including the Expert Report of Professor David Cutler, dated March 25, 2019 ("Cutler Report"); the Expert Report of Professor Jonathan Gruber, dated March 25, 2019 ("Gruber Report"); the Expert Report of Craig J. McCann, Ph.D., CFA, dated March 25, 2019 ("McCann Report"); the Expert Report of Katherine M. Keyes, Ph.D., MPH, dated March 25, 2019 ("Keyes Report"); the Supplemental Expert Witness Report of G. Caleb Alexander, MD MS, dated April 3, 2019 ("Alexander Report"); and the Supplemental Expert Report of Dr. Jeffrey B. Liebman, dated April 3, 2019 ("Liebman Report").

7. I am asked by counsel for Distributors[6] to address, from the perspective of an economist specializing in the pharmaceutical industry, whether Plaintiffs have reliably established a causal chain from the alleged conduct on the part of Distributors to the alleged health-related outcomes underlying the Plaintiffs' liability and damages claims. I also am asked to respond to certain opinions presented in the Cutler, Gruber, McCann, Keyes, Alexander, and Liebman Reports, as appropriate.

8. The materials that I or individuals working under my direction have considered are noted in Exhibit I-2. I understand that discovery is ongoing in this matter and that certain information may be updated or that additional documents or materials

---

4 See e.g., Summit Complaint, ¶ 498; Cuyahoga Complaint, ¶ 466.

5 See e.g., Summit Complaint, ¶¶ 714-745; Cuyahoga Complaint, ¶¶ 715-770.

6 I am advised that the Defendants on whose behalf I am submitting this report could change.

may be subsequently created or provided. Accordingly, I reserve the right to supplement or modify my opinion, if warranted, as additional information or documents are made available to me. Such additional information includes, without limitation, testimony of Plaintiffs' expert witness Dr. McCann, which was not completed in time to be considered for purposes of this report. In addition, I reserve the right to prepare additional supporting materials such as summaries, graphical exhibits, charts, demonstratives, animations, enlargements, or other enhancements, including for hearings and trial. I also reserve the right to use at hearings, including trial, any supporting materials, such as summaries, graphical exhibits, or charts, from any of the materials or data referenced in my report or the appendices attached hereto in addition to documents produced in this litigation that refer to or relate to the opinions in my report.

9. My report is organized as follows. Section II provides a summary of my opinions. Section III contains background information on the pharmaceutical treatment of pain, including the prescription opioid category and its relevant regulatory environment. I provide an overview of the distribution of prescription pharmaceuticals in section IV, including the flow of payments and information associated with the distribution of prescription opioids. Section V introduces substance abuse, including abuse of prescription and non-prescription opioids. The diversion of prescription opioids is summarized in section VI, along with challenges associated with its detection by Distributors. Section VII discusses the effectiveness of certain Distributor actions on diversion. Section VIII provides a discussion of certain flaws associated with Plaintiffs' assertion of a causal chain between the actions taken (or not taken) by Distributors and the asserted adverse health outcomes within the Counties. Section IX contains my assessment of certain opinions presented in the Gruber, Cutler, and McCann Reports. Section X considers issues relating to abatement of alleged opioid-related harms and my assessment of certain opinions presented in the Keyes, Alexander, and Liebman Reports.

II. SUMMARY OF OPINIONS

10. My opinions are described throughout this report, but for ease of reference I summarize some of the key opinions here. My opinions are proffered to a reasonable degree of professional certainty.

11. Plaintiffs assert that large volumes of prescription opioids shipped by Distributors were diverted for illegitimate non-medical use. As I understand it, Plaintiffs' theory is that Distributors, by monitoring the orders they received from pharmacies, should have detected within those orders any such diversion, and should have prevented diversion by reporting more orders than they did to the U.S. Drug Enforcement Administration ("DEA") and/or by refusing to fill orders that would be diverted to an illegitimate non-medical use. It is my opinion, however, that there are significant flaws with various links in the causal chain that Plaintiffs seek to forge.

12. First, Distributors have limited ability to identify diversion within the large volumes of orders that are presumptively intended for legitimate medical use.

    (a) Plaintiffs claim that Distributors delivered more opioids into communities than would be consistent with legitimate medical needs. Yet while each individual Distributor was able to monitor orders it received from its pharmacy customers, those Distributors without pharmacy operations typically had no visibility into those same customers' transactions with other distributors and manufacturers, or the transactions of pharmacies who were not its customers.[7] Thus, individual Distributors had only an incomplete picture by which they could discern overall patterns and volumes of deliveries to the Counties.

[7] Distributors with pharmacy operations could observe what affiliated pharmacies were ordering from other distributors and manufacturers, but could not observe what unaffiliated pharmacy customers were ordering from other distributors and manufacturers.

(b) Plaintiffs claim that Distributors should have readily identified suspicious orders based on the size and pattern of orders by individual pharmacies. Yet variability in pharmacy ordering is the norm, and fluctuations from any arbitrarily chosen baseline level do not support an inference of diversion. For example, some pharmacies serve a large base of patients, and some a smaller base. Accordingly, one can expect different volumes of orders among pharmacies, complicating the identification of diversion on the basis of an individual Distributor's own orders and deliveries. Likewise, variability in the volumes of prescription opioids ordered by any individual pharmacy from time period to time period is typical, particularly given the launch of new products. Underlying these sources of variability is an additional level of variation in prescribing (including the uncertain impact of new prescribing guidelines), which may change over time and across categories of prescribers, and as a community's medical needs evolve.

(c) Additionally, the prescription opioid volumes accounted for by patients apparently seeking prescriptions from many doctors, and/or filling prescriptions at many pharmacies, are a small fraction of overall prescribing volumes in the Counties.

(d) Accordingly, if prescribing and/or dispensing associated with a given pharmacy were "too high" because of diversion, these volumes are likely to be masked by the volume of legitimate prescriptions being filled at the same pharmacy. Any diversion would be hard to detect given the variability of legitimate shipments.

13. In contrast to the paucity of information available to individual Distributors, state and federal agencies did have more comprehensive information that could be used to identify diversion. Further, these agencies also had enforcement powers to eliminate sources of diversion in a sustained manner.

(a) Every order for controlled substances is reported to the DEA. As such, the DEA has the information on total shipments into the Counties and the ability to investigate and strip pharmacies of their ability to handle controlled substances. Further, it was the DEA that considered utilization and increased the quota of controlled substances that could be made available in the U.S., thus enabling the increase in the use of prescription opioids.

(b) Ohio's Board of Pharmacy ("BOP") runs the state's Prescription Drug Monitoring Program ("PDMP"). The Ohio Automated Rx Reporting System ("OARRS") database has tracked every prescription from every prescriber dispensed for every patient since 2006. Thus, Ohio's BOP was in a position to investigate and identify healthcare practitioners ("HCPs") that may have been over-prescribing opioids, patients who were being dispensed excessive amounts of opioids, and pharmacies that were not appropriately assessing the volume of prescription dispensed to patients. As all pharmacies must maintain their licenses with Ohio's BOP and all physicians must maintain their licenses with Ohio's State Medical Board ("SMB"), these organizations had the ability to strip physicians of their ability to prescribe opioids and pharmacies of their ability to dispense opioids.

(c) Ohio's Medicaid program (administered by the Ohio Department of Medicaid ("Ohio Medicaid")) also observed and adjudicated the claims for opioid prescriptions written for their covered patients. Similarly, Ohio's Bureau of Workers' Compensation ("WCB") observed and adjudicated the claims for prescription opioids associated with their purview.

14. Second, it is not apparent that increased reporting and/or blocking of orders by Distributors would have reduced diversion without also imposing a significant burden on the legitimate medical needs for pain relief experienced by thousands of patients in the Counties. The reporting of a "suspicious" order to the DEA

rarely results in the loss of the pharmacy's DEA registration to dispense controlled substances. At least [redacted] orders from pharmacies in the Counties were reported by distributors to the DEA as suspicious; it is not apparent that any change in pharmacy ordering of opioids ensued. In contrast, shipments by Distributors were in response to orders from pharmacies registered with the DEA to handle controlled substances. Given the small amounts of suspected doctor and pharmacy shopping, it would appear that the vast majority of pharmacy orders were the result of legitimate prescriptions, presumably written for patients with real medical needs by HCPs who also were appropriately registered with the DEA. Blocking orders would have prevented those patients from accessing medically approved treatment for pain.

15. It was understood that untreated (or ineffectively treated) pain imposes significant costs. Pharmaceutical treatments for pain, including prescription opioids, are important elements in the protocols used by HCPs to enable pain sufferers to lead more fulfilling and productive lives. In recognition of this, the DEA determined that it was appropriate to increase the quota of controlled substances that could be made available in the U.S., thus enabling the increase in the use of prescription opioids. In this context, Distributors failing to ship orders would appear to be an overly blunt instrument, potentially depriving legitimate patients of needed treatment. Individual Distributors had only their own information to consider and were not in a position to second-guess the prescribing decisions of HCPs that led to the pharmacy orders that Distributors were asked to ship.

16. Third, Plaintiffs seek to link prescription opioid shipments by Distributors to a wide range of costs allegedly stemming from opioid use (and abuse), including use of illicit opioids such as heroin and the 10 to 50 times more potent fentanyl and its analogues, particularly carfentanil. Drug and substance abuse, however, is a long-standing, complex phenomenon with multiple causes. Many individuals who used prescription opioids non-medically had already abused drugs, or had proclivities for drug abuse, prior to receiving prescription opioids. Accordingly, it

is not apparent that the availability of prescription opioids led to associated harms that otherwise would not have occurred.

(a) Drug and substance abuse is not a new phenomenon. It has been increasing in the U.S. since at least the late 1970s. It did not begin with the increased use of prescription opioids. Plaintiffs appear to claim that the actions of Distributors led to drug abuse in individuals that would otherwise not have occurred; the information available does not support that claim.

(b) Plaintiffs appear to claim there is a well-worn path from legitimate prescription opioid use, to non-medical use, to use of illicit substances such as heroin and fentanyl, and then on to overdose and death. This, however, is a rare circumstance, and one in which numerous other factors come into play. The percentage of patients prescribed an opioid who later go on to abuse and/or overdose on heroin is very low, by various accounts less than 1 percent. Therefore, it is apparent that other factors beyond the initial prescription opioid use are causally related to the use of illicit opioids.

(c) Individuals using prescription opioids non-medically have characteristics that distinguish them from typical patients prescribed opioids. These individuals who go on to use opioids non-medically are also more likely to abuse other substances, and are also more likely to suffer from mental health conditions and other ailments. By way of example, older women represent the group most likely to be prescribed opioids; the individuals who most often suffer overdoses from heroin and fentanyl tend to be younger men. Further, opioid abuse is correlated at the local level with underlying economic factors that would have existed, and that would have been risk factors for higher drug abuse levels, whether or not Distributors reported and/or failed to ship more orders.

17. My opinions with respect to the Gruber Report are as follows.

(a) The Gruber Report asserts a causal link between prescription opioid shipments and opioid misuse and mortality. Yet the Gruber Report does not demonstrate that the allegedly "excessive and unnecessary" shipments resulted from illegitimate, non-medical use, nor does it substantiate that these shipments are unrelated to medical need.

(b) The Gruber Report posits a relationship between prescription opioid shipments and alleged illicit opioid mortality. The Gruber Report, however, fails to support the claim that the trend in illicit opioid mortality after 2010 was caused by the formation of a "stock of individuals" generated prior to 2010 as a result of Distributors' "excessive and unnecessary" shipments. Further, the Gruber Report does not explain how Distributors' conduct resulted in a "direct, causal relationship" with illicit opioid mortality when various other factors outside Distributors' control had an effect on illicit opioid use.

(c) The Gruber Report asserts an immaterial relationship between opioid-related mortality and economic conditions, on the basis of a selective and misleading review of certain academic articles. To the contrary, there is an established link between opioid-related mortality and long-run economic conditions.

18. My opinions with respect to the Cutler Report are as follows.

(a) The Cutler Report purports to identify and compute the effect of prescription opioid shipments on harms that resulted in costs to the Counties. The attempt to compute the share of harms allegedly attributable to opioids assumes, erroneously, that in a world in which opioids were either not present, or were present to a reduced degree, these harms would not exist. As noted above, drug and substance abuse has

been a scourge on the U.S. for decades. The phenomenon did not begin with the broad availability of prescription opioids.

(b) The empirical models proposed to estimate the relationship between shipments and opioid-related mortality are based on flawed premises.

(i) The "direct approach" seeks to estimate the relationship between changes in county-level mortality and the average level of per-capita shipments to the county through 2010, controlling for certain economic and demographic characteristics of the county. Yet shipments depend on prescribing, and the Cutler Report does not identify how Distributors are expected to monitor or question prescribing decisions.

(ii) The "indirect approach" attempts to estimate the relationship between mortality and economic and demographic characteristics in a period preceding the alleged misconduct, and uses the estimated model to predict the mortality that would have been expected in the absence of the alleged misconduct. This approach embeds a strong form of the "gateway" assumption that links prescription opioid use to illicit opioid use, without adjusting for those individuals who would have used illicit opioids in the absence of prescription opioids. It also attributes all of the residual harms in the post-2010 period to Defendants, notwithstanding the acknowledgement that policies outside the control of Distributors contributed to the increased use of illicit opioids, while also ignoring any baseline level of illicit opioid use that would be unrelated to shipments.[8]

[8] At his deposition, Professor Cutler appeared to reduce his reliance on the "gateway" hypothesis, articulating instead a "thick market" explanation which likewise is not supported (Deposition of David Cutler, Ph.D., April 26, 2019 ("Cutler Deposition Day 1"), pp. 321-322).

(iii) The Cutler Report fails to account for important factors affecting mortality, such as the lower cost and increased lethality of fentanyl and its analogues, including carfentanil, making mortality a poor proxy for consequences of improper prescription opioid use and thus breaking the chain of alleged causality between opioid shipments and damages and death due to illicit opioids.

19. My opinions with respect to the McCann Report are as follows.

(a) The McCann Report develops certain analyses to identify allegedly "suspicious" orders, including implementing an instruction of counsel for Plaintiffs. These approaches lead to results that lack credibility, including conclusions that up to 83 percent of shipments should have been blocked. The McCann Report reaches these conclusions apparently without consideration for the legitimate medical needs of patients or without consideration for the various reasons that the thresholds would not identify actual orders that should be blocked.

(b) The McCann Report's analysis of allegedly excessive overall shipments adopts an oversimplified approach. The proposed "lower bound" for a "baseline" of medically necessary per capita shipments is unable to account for important changes to the market environment that occurred after 1997, while the proposed "upper bound" for a "baseline" of medically necessary per capita shipments assumes without support that the proposed evolution to the 2018 opioid utilization levels adequately would meet patient needs.

20. Plaintiffs identify a variety of abatement measures, the costs of which are asserted as necessary in order to address the alleged current and future harms as a result of Distributors' actions. These issues are addressed by the Keyes, Alexander, and Liebman Reports. My opinions with respect to the issues of abatement, future harms, and the Keyes, Alexander, and Liebman Reports are as follows.

(a) Considering a number of metrics, prescription opioid misuse has peaked in the Counties and is starting to decline. As a result, Plaintiffs' claims of future damages based on a constant stock of patients are overstated.

(b) Plaintiffs claim that a number of abatement measures will be necessary in the Counties in order to reverse opioid-related morbidity and mortality, and that the provision of these abatement measures will impose a significant financial burden on the Counties. Plaintiffs neglect to consider, however, the many federal programs that are already funded and providing the abatement measures that Plaintiffs claim. These include Federal programs for treatment, prevention, and harm reduction.

(c) As examples, Plaintiffs claim costs for the provision of treatment and support services for addicted individuals and neonatal abstinence syndrome ("NAS"). The conditions under which any of these costs would be borne by the Counties is not evident. For instance, the treatment costs of both overdose and NAS may be covered by Medicaid, which would impose no additional financial burden on the Counties. Further, my own analysis of Medicaid data suggests that the median incremental cost borne by Medicaid and associated with treatment of opioid abuse or dependence could be approximately $2,663.

III. BACKGROUND

A. Pain

21. Pain is reported to be a major reason for Americans to seek medical care.[9] According to the National Health Interview Survey ("NHIS"), most Americans have suffered from mild to severe levels of pain at some time in their lives.[10]

---

[9] See, for example, St. Sauver, Jennifer L. et al., "Why do patients visit their doctors? Assessing the most prevalent conditions in a defined US population," *Mayo Clinic Proceedings*, 88:1, 2013, p. 5; Galluzzi, Katherine E., "Management of Neuropathic Pain," *Journal of the American Osteopathic Association*, 105:9, 2005, p. S12.

[10] "NIH Analysis Shows Americans Are in Pain," National Center for Complementary and Integrative Health Press Release, August 11, 2015, https://nccih nih.gov/news/press/08112015.

Survey estimates from 2016 indicate that 50.0 million U.S. adults suffered from chronic pain on most days or every day in the past 6 months, with 19.6 million suffering from chronic pain that limited life or work activities on most days or every day in the past 6 months.[11]

22. Pain can be classified based on duration as acute or chronic. Acute pain starts suddenly and lasts for a short period; chronic pain persists over time. Acute pain can be caused by surgery, broken bones, or dental work; chronic pain may be due to arthritis, cancer, or nerve pain.[12] Chronic pain typically becomes more common and problematic with age. Among all known causes of chronic pain, low back pain and osteoarthritis are the most frequent.[13]

23. Pain is also classified by severity: mild, moderate, or severe. The World Health Organization ("WHO") developed a "Pain Ladder" in 1986 to inform cancer pain treatment options. According to the WHO, when pain first occurs, patients are advised to start with non-opioid medications such as aspirin for mild pain. If pain persists, mild opioids can be used for mild to moderate pain, as necessary, with stronger opioids for severe pain.[14]

24. Pain is also classified as either nociceptive or neuropathic. Nociceptive pain is the most common type of pain and results from the body reacting to potentially harmful stimuli such as heat, sharp objects, or broken bones. The sources of nociceptive pain are generally easy to identify.[15] In comparison, neuropathic pain

---

11 Dahlhammer, James, et al., "Prevalence of chronic pain and high-impact chronic pain among adults—United States, 2016," *Morbidity and Mortality Weekly Report*, 67:36, 2018, p. 1002.

12 "Acute vs. Chronic Pain," Cleveland Clinic, https://my.clevelandclinic.org/health/articles/12051-acute-vs-chronic-pain.

13 "Chronic Pain: In Depth," National Institutes of Health ("NIH"), https://nccih nih.gov/health/pain/chronic.htm#hed2.

14 "WHO's cancer pain ladder for adults," WHO, https://www.who.int/cancer/palliative/painladder/en/. See also "WHO Pain Ladder with Pain Management Guidelines," South West Regional Wound Care Toolkit, https://www.southwesthealthline.ca/healthlibrary_docs/B.5.3.WHOPainLadder.pdf.

15 "Nociceptive Pain," Healthline, https://www.healthline.com/health/nociceptive-pain; Watson, James C., "Nociceptive Pain," Merck Manual: Consumer Edition, https://www merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/pain/nociceptive-pain.

occurs when nerve fibers are damaged or injured. Examples of conditions that are often associated with neuropathic pain are diabetes, herpes zoster infection, and cancer.[16] It has been estimated that up to 10 percent of the U.S. population suffers from neuropathic pain.[17] The causes of neuropathic pain are not always easily identifiable.[18]

(a) Costs of Pain

25. Pain, and especially chronic pain, can have a negative impact on many aspects of a patient's quality of life. Physically, pain is associated with difficulty sleeping, increased fatigue, and decreased physical functioning.[19] Psychologically, pain is related to high levels of anxiety, depression, and cognitive impairment.[20] Socially, pain is associated with feelings of social anxiety and occupational dysfunction (e.g., reduced capacity to work), interference with everyday activities such as home responsibilities and exercise, and detriment to a patient's family (e.g., by causing family members to provide additional care for the patient).[21] Pain has such a significant impact on a person's quality of life that some argue pain relief is a universal human right under international law.[22] The burdens of

---

16 Campbell, James N., and Richard A., Meyer, "Mechanisms of Neuropathic Pain," *Neuron*, 52:1, 2006, p. 77.

17 DiBonaventura, M. D. et al., "The prevalence of probable neuropathic pain in the US: results from a multimodal general-population health survey," *Journal of Pain Research*, 10, 2017, pp. 2525-2538.

18 See, for example, "Neuropathic Pain Management," WebMD, https://www.webmd.com/pain-management/guide/neuropathic-pain#1.

19 See, for example, Phillips, Ceri J., "The cost and burden of chronic pain," *Reviews in Pain*, 3:1, 2009, ("Phillips 2009"), p. 3; Dueñas, Maria et al., "A review of chronic pain impact on patients, their social environment and the health care system," *Journal of Pain Research*, 2016, 9 ("Dueñas et al. 2016"), Figure 1; Muneer, Sabby, "Socioeconomic Burden of Chronic Pain," *Faculty Perspectives in Chronic Pain: Socioeconomic Burden of Chronic Pain*, 2016, ("Muneer 2016"), p. 3.

20 Phillips 2009, p. 3; Lame, Inge E. et al., "Chapter 2: Quality of life in chronic pain is more associated with beliefs about pain than with pain intensity," *Psychological predictors and treatment outcome in chronic pain*, 2005 ("Lame et al. 2005"), p. 26; Muneer 2016, p. 4.

21 Breivik, Harald et al., "The individual and societal burden of chronic pain in Europe: the case for strategic prioritisation and action to improve knowledge and availability of appropriate care," *BioMed Central Public Health*, 13, 2013, p. 1229; Dueñas et al. 2016.

22 Cousins, Michael J. et al., "Pain relief: a universal human right," *Pain*, 112:1, 2004, p. 3; Lohman, Diederik, Rebecca Schleifer, and Joseph J Amon, "Access to pain treatment as a human right," *BioMed Central Medicine*, 8:8, 2010, pp. 5-6.

pain are numerous and significant; for many, the burden can become unbearable. Chronic pain is a significant risk factor for suicide, with one study suggesting that half of all patients with chronic pain have serious suicidal thoughts.[23]

26. Pain is also associated with substantial financial costs, both in terms of medical treatments, and lost wages and economic output.[24] Every year, U.S. adults with moderate pain spend an average of $4,516 more on health care than adults without pain; adults with severe pain spend an additional $3,210, on average.[25] These average differences could also be driven by other health factors correlated with pain, such as age and other underlying health conditions. Using an analysis that attempts to account for these differences, one study estimates that the annual incremental costs associated with pain range from $2,600-$3,000 per affected individual, for a total annualized cost of $261-$300 billion in the U.S.[26] Furthermore, chronic pain is recognized as a major health problem, producing significant social burden on various governmental agencies,[27] such as children's services.

27. Researchers have also estimated the annual direct costs per patient associated with specific conditions:

(a) The average annual costs associated with osteoarthritis pain are an estimated $3,702;[28]

---

23 Martin D. Cheatle, "Depression, Chronic Pain, and Suicide by Overdose: On the Edge," *Pain Medicine*, 12, 2011, p. 44; Ilgen, Mark A. et al., "Noncancer Pain Conditions and Risk of Suicide," *Journal of American Medical Association Psychiatry*, 70:7, 2013, p. 695.

24 Committee on Advancing Pain Research, Care, and Education, "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research," *The National Academies Press* ("Relieving Pain in America"), p. 56; Stewart, Walter F.et al., "Lost Productive Time and Cost Due to Common Pain Conditions in the US Workforce," *Journal of the American Medical Association*, 290:18, 2003, ("Stewart et al. 2003"), p. 2446.

25 Gaskin, Darrell J. and Patrick Richard, "The Economic Costs of Pain in the United States," *The Journal of Pain*, 13:8, 2012, ("Gaskin and Richard 2012"), p. 719.

26 Gaskin and Richard 2012, p. 720.

27 Dueñas et al. 2016, p. 457.

28 Di Bonaventura, Marco da Costa et al., "Evaluating the health and economic impact of osteoarthritis pain in the workforce: results from the National Health and Wellness Survey," *BioMed Central Musculoskeletal Disorders*, 12, 2011, p. 5.

(b) The average annual costs associated with post-herpetic neuralgia were an estimated $10,206;[29]

(c) The average annual costs associated with painful diabetic peripheral neuropathy were an estimated $22,754;[30] and

(d) The average annual pain-related costs associated with nerve damage from spinal cord injury is an estimated $8,636.[31]

28. The financial burden of pain is magnified by the fact that pain is typically associated with lost income via a decreased ability to work, leading to lost days of work, reduced work hours, and potentially lower hourly wages. In total, these annualized economic costs are estimated to range from $300-$335 billion per year in the U.S.[32] Furthermore, this estimate does not consider lost productivity during actual work hours.

29. Researchers have also estimated the lost income associated with a variety of specific conditions:

(a) Back pain is associated with indirect costs ranging from $26-$159 billion;[33]

(b) The total costs due to missed work days associated with osteoarthritis are an estimated $10.3 billion;[34]

---

29 Dworkin, Robert H. et al., "Impact of postherpetic neuralgia and painful diabetic peripheral neuropathy on healthcare costs," *Journal of Pain*, 10:4, 2009 ("Dworkin 2009"), p. S17.

30 Dworkin 2009, p. S17.

31 Mann, R, Caroline et al., "Burden of spinal cord injury-related neuropathic pain in the United States: retrospective chart review and cross-sectional survey," *Spinal Cord*, 51, 2013, p. 568.

32 Gaskin and Richard 2012, p. 722.

33 Ma, Vincent Y, et al., "Incidence, Prevalence, Costs, and Impact on Disability of Common Conditions Requiring Rehabilitation in the United States: Stroke, Spinal Cord Injury, Traumatic Brain Injury, Multiple Sclerosis, Osteoarthritis, Rheumatoid Arthritis, Limb Loss, and Back Pain," *Archives of Physical Medicine and Rehabilitation*, 95, 2014, ("Ma et al. 2014"), p. 987.

34 Ma et al. 2014, pp. 987-988.

(c) The indirect costs associated with rheumatoid arthritis total an estimated $13 billion in 2013 dollars;[35] and

(d) Arthritis in general is estimated to result in the loss of 5.2 productive hours a week for each affected employee.[36]

30. Overall, the total costs of pain are estimated to range from $560-$635 billion per year in the U.S., covering the dual burdens of an increase in medical expenses coupled with the reduction in ability to work.[37] These significant financial costs along with the physical costs discussed above imply an immense burden of pain.

(b) Treating Pain

31. Pain management is an important part of the practice of many HCPs, in particular including those treating arthritis and cancer patients. Over time, the treatment of pain has evolved into a recognized specialty, pain medicine, within which board-certified HCPs focus on treating the particularly problematic manifestations of pain.[38]

32. Pain management clinics ("PMCs") tend to be either multi-disciplinary health care facilities where providers use a variety of approaches to treat pain or PMCs may be focused on certain types of procedures, such as injections or nerve blocks. Reflecting a holistic perspective on the treatment of pain and cognizant of the encompassing impact of the condition, PMCs may include physical and occupational therapists, psychologists, and dietitians, providing a broad array of

35 Ma et al. 2014, p. 988.

36 Stewart, Walter F. et al., "Lost Productive Time and Cost Due to Common Pain Conditions in the US Workforce," *Journal American Medical Association*, 290:18, 2003, p. 2446.

37 Gaskin and Richard 2012, pp. 722-723.

38 Upp, Justin et al., "The Evolution and Practice of Acute Pain Medicine," Pain Medicine, 2013, 14:1, pp. 124-144; "Pain Medicine (PM) Examination," The American Board of Anesthesiology, http://www.theaba.org/Exams/Pain-Medicine-Certification/Pain-Medicine-Certification; "Pain Medicine," American Board of Physical Medicine and Rehabilitation, https://www.abpmr.org/subspecialties/pain; "American Board of Pain Medicine," https://www.abpm.org.

complementary approaches to pain management, including, among others, acupuncture, cognitive behavioral therapy, massage, and meditation.[39]

33. Pain treatments may be pharmacological or non-pharmacological. Examples of non-pharmacological treatments include physical therapy, surgery, and medical devices, such as transcutaneous electrical nerve stimulation ("TENS").[40] Pharmaceutical treatments for pain include aspirin, acetaminophen (e.g., Tylenol), non-steroidal anti-inflammatory drugs ("NSAIDs") (e.g., Advil, Aleve), local anesthetics (e.g., Lidoderm), muscle relaxants (e.g., Flexeril), and opioids.[41] Some of these products are available only by prescription; others are also available, typically at a lower strength, without a prescription as over-the-counter ("OTC") products. Some are available only as branded products and others are available in one form or another as generics.

34. There have been several official recognitions of the undertreatment of pain. In October 2000, the U.S. House of Representatives passed the "Pain Relief Promotion Act" (the "PRPA") that called for, "a new emphasis on pain management and palliative care."[42] The goal of the PRPA was to draw "greater attention among scientists and practitioners into pain management and research."[43] The PRPA states that "inadequate treatment of pain, especially for chronic diseases and conditions, irreversible diseases such as cancer, and end-of-

---

39 "Pain Management Clinic," CIGNA, https://www.cigna.com/individuals-families/health-wellness/hw/medical-topics/pain-management-clinic-tr3230; "Is a Pain Clinic Right for You?," Arthritis Foundation, https://www.arthritis.org/living-with-arthritis/pain-management/chronic-pain/pain-clinic.php; "Pain Centers," Institute for Chronic Pain, http://www.instituteforchronicpain.org/treating-common-pain/pain-centers.

40 "FDA Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain," U.S. Food and Drug Administration ("FDA"), September 2018, https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_analgesic_2018_09_18_FDA_Blueprint.pdf, p. 7; DeSantana, Josimari M. et al., "Effectiveness of Transcutaneous Electrical Nerve Stimulation for Treatment of Hyperalgesia and Pain," *Current Rheumatology Reports*, 10:6, p. 492.

41 Blondell, Richard D. et al., "Pharmacologic Therapy for Acute Pain," *American Academy of Family Physicians*, 87:11, 2013, pp. 766-772; "Pain Relievers," MedlinePlus, https://medlineplus.gov/painrelievers html.

42 The Pain Relief Promotion Act (H.R. 2260), Senate Report 106-299, 106th Congress, 2nd Session, May 23, 2000 ("PRPA Senate Report"), p. 2. The PRPA was not passed by the Senate into law.

43 PRPA, Senate Report, p. 6.

life care, is a serious public health problem affecting hundreds of thousands of patients every year."[44] Additionally, the PRPA states:

> 35. the dispensing or distribution of certain controlled substances for the purpose of relieving pain and discomfort even if it increases the risk of death is a legitimate medical purpose and is permissible under the Controlled Substances Act… [P]hysicians should not hesitate to dispense or distribute controlled substances when medically indicated…[45]

36. The Joint Commission (formally the Joint Commission on Accreditation of Healthcare Organizations) is the national accreditor of over 20,000 healthcare organizations and programs in the US.[46] In 2000, the Joint Commission introduced pain management standards for healthcare organizations.[47] The standards emphasized the need for organizations to undertake systematic assessments and use quantitative measures of pain (e.g., using a 10-point scale) and provided "examples of implementation" which highlight how organizations can successfully meet the standards.[48]

37. Additional statements supporting the undertreatment of pain include the following.

(a) A 2001 consensus statement by the DEA and 21 health organizations, notes, "Undertreatment of pain is a serious problem in the United States, including pain among patients with chronic conditions and those who are critically ill or near death … and pain should be treated aggressively." "For many patients, opioid analgesics – when used as recommended by established pain management guidelines – are the most effective way to

---

44 PRPA, Senate Report, p. 2.

45 The Pain Relief Promotion Act (H.R. 2260), Senate Report 106-299, 106th Congress, 2nd Session, May 23, 2000, p. 2.

46 "About the Joint Commission", The Joint Commission, https://www.jointcommission.org/about_us/about_the_joint_commission_main.aspx; Baker, David W., "History of The Joint Commission's Pain Standards: Lessons for Today's Prescription Opioid Epidemic," *JAMA*, 317:11, 2017, ("Baker 2017"), p. E1.

47 Philips, Donald M., "JCAHO Pain Management Standards Are Unveiled," *JAMA*, 284:4, 2000, pp. 428-429.

48 Baker 2017, p. E1.

treat their pain, and often the only treatment option that provides significant relief."[49]

(b) The Ohio Intractable Pain Act of 1998 provides authority for physicians to prescribe, dispense, and administer "dangerous drugs" (i.e. prescription drugs)[50] for the management of intractable pain in amounts or combinations that may not be appropriate when treating other medical conditions. It calls for the SMB to establish standards and procedures for diagnosis and treatment.[51] The Ohio Prescription Drug Abuse Task Force found that "Growing recognition by professionals of the under-treatment of pain in the late 1990's prompted needed changes in clinical pain management guidelines at the national level, as well as changes in Ohio's law regarding the treatment of intractable pain."[52]

(c) The 2004 Report of the Ohio Compassionate Care Task Force found that "fear and misunderstanding of the existing statutes and rules regarding prescribing of opioid medications interfere with appropriate pain and symptom management" and "fear of regulatory scrutiny and litigation interfere with providing appropriate care." The Ohio Compassionate Care Task Force was created for the purpose of studying and making recommendations concerning the treatment and care of persons with terminal illness or severe chronic pain.[53]

---

49 "Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act," A Joint Statement From 21 Health Organizations and the DEA, October 2001, http://www.aspmn.org/documents/A_JOINT_STATEMENT_FROM_21_HEALTH_ORGANIZATIONS.pdf. Participating health organizations include the American Academy of Family Physicians, American Cancer Society, American Medical Association, and the American Society of Anesthesiologists, among others.

50 Ohio Revised Code, § 4729.01, http://codes.ohio.gov/orc/4729.

51 "An Act to enact sections 4731.052 and 4731.283 of the Revised Code regarding the authority of physicians to prescribe, dispense, and administer dangerous drugs for management of intractable pain," 122nd General Assembly, Substitute House Bill Number 187.

52 "Ohio Prescription Drug Abuse Task Force: Final Report Task Force Recommendations," Ohio Prescription Drug Abuse Taskforce, October 1, 2010, p. 22.

53 "Report of the Ohio Compassionate Care Task Force," Ohio Compassionate Care Task Force, March 2004, pp. 5, 12-13.

38. In conclusion, it has been widely recognized that chronic pain, when left untreated, has significant consequences for an individual's physical and mental health, causing a deterioration in the quality of life for individuals and those close to them.[54] In addition, pain imposes a significant financial burden on the patient and society.[55]

B. Opioids

(a) Overview

39. Prescription opioids are powerful analgesics that are frequently used for the treatment of acute pain (e.g., occurring after surgery or injuries) and for chronic pain due to cancer and other serious conditions. As shown on Exhibit III-1, these products include a number of natural substances and their semi-synthetic analogues, such as morphine, oxymorphone, oxycodone, hydromorphone, and hydrocodone.[56]

40. Short-acting or immediate-release formulations of prescription opioids are taken every 3 to 4 hours or as needed for the treatment of acute pain or break-through flares in a chronic pain situation.[57] For example, the recommended dosage of a combination hydrocodone and acetaminophen formulation (e.g., Vicodin) is one to two 5/500 mg tablets every four to six hours.[58] In contrast, long-acting opioid ("LAO") analgesics, also called controlled-release or extended-release opioid formulations, tend to be dosed over longer intervals (e.g., every 12 hours).[59] For example, the recommended dose of OxyContin is 10 mg, twice a day.[60] The

---

54 Dueñas et al. 2016, p. 464.

55 Dueñas et al. 2016, pp. 457, 464.

56 Watson, James C., "Treatment of Pain," Merck Manual: Professional Version, https://www merckmanuals.com/professional/neurologic-disorders/pain/treatment-of-pain.

57 "ACPA Resources Guide to Chronic Pain Management," American Chronic Pain Association, 2018, ("ACPA"), pp. 87-88.

58 Vicodin product insert label, approved December 26, 2006, https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/088058s027lbl.pdf.

59 ACPA, p. 88.

60 OxyContin product insert label, approved September 26, 2018, https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022272s039lbl.pdf.

advantage of LAOs tends to be a more stable extended level of pain relief with a reduced pill burden and better nighttime pain control.[61] As discussed above, better pain management can improve the patient's quality of life.[62]

41. Prescription opioids have different potencies depending on their active ingredient. Accordingly, comparisons across opioids may be based on milligram morphine equivalents ("MMEs"), which is determined by using a factor to calculate a dose of morphine that is equivalent to the opioid in question. More potent opioids are associated with higher MME conversion factors; for example, a 100 mg dose of morphine is equivalent to a 65 mg dose of oxycodone and a 37 mcg/hr dose of fentanyl.[63]

42. Over time, repeated administration of prescription opioids may result in a tolerance, where the individual no longer responds to the drug in the way they initially did.[64] As this tolerance develops, practitioners may adjust treatment in order to achieve the desired therapeutic effect. Examples include increasing the dose, reducing the interval between doses, or both.[65] Nonetheless, higher and/or more frequent doses of opioids can be associated with a greater risk of overdose, which may be fatal due to respiratory depression.[66]

---

61 See, for example, Nicholson, Bruce, "Benefits of Extended-Release Opioid Analgesic Formulations in the Treatment of Chronic Pain," *Pain Practice*, 9:1, 2009, p. 71; Argoff, Charles E. and Daniel I. Silvershein, "A Comparison of Long- and Short-Acting Opioids for the Treatment of Chronic Noncancer Pain: Tailoring Therapy to Meet Patient Needs," *Mayo Clinic Proceedings*, 84:7, 2009, pp. 603, 609.

62 Katz, Nathaniel, "The Impact of Pain Management on Quality of Life," *Journal of Pain and Symptom Management,* 24:IS, 2002, p. S38.

63 See e.g., "Morphine Equivalent Dosing," Wolters Kluwer, https://www.wolterskluwercdi.com/sites/default/files/documents/ebooks/morphine-equivalent-dosing-ebook.pdf?v3, p. 3.

64 Cami, Jordi et al., "Drug Addiction," *The New England Journal of Medicine*, 349:10, 2003, ("Cami et al. 2003"), pp. 977, 982; "6: Definition of tolerance," NIH, https://www.drugabuse.gov/publications/teaching-packets/neurobiology-drug-addiction/section-iii-action-heroin-morphine/6-definition-tolerance.

65 Cami et al. 2003, pp. 977, 982.

66 "Information sheet on opioid overdose," World Health Organization, https://www.who.int/substance_abuse/information-sheet/en/.

43. I understand that opioid use may generate a feeling of euphoria and as such opioids may be subject to misuse and abuse.[67] Another facet of opioid misuse and abuse is the physical dependence that may emerge if a patient is prescribed opioid analgesics for a period of time, particularly if the patient has risk factors for substance abuse. Once physical dependence develops, non-fatal withdrawal symptoms may include: anxiety, craving for the drug, increased respiratory rate, sweating, cramps, tremors, twitching, fever and chills, and nausea.[68] As a result, patients may seek to continue consumption of the opioid analgesic even though the underlying pain, for which the medication may have been initially prescribed, has diminished.

(b) Timeline of Opioid Products

44. Natural opioids are derived from alkaloids taken from the opium poppy. Morphine, a natural opioid, was the first opioid to be marketed commercially. Isolated in the early 1800s, Merck Laboratories began to market morphine in the U.S. in 1827.[69] In 1898, the Bayer Company began marketing a more potent form of morphine, diacetylmorphine, as Heroin; it was prescribed for almost all illnesses for which codeine or morphine was used. Heroin was made illegal in the U.S. in 1924.[70]

45. Additional opioids were isolated in the 20th century. Oxycodone was first synthesized in 1916; hydrocodone was produced in 1920; hydromorphone was synthesized in 1921; and fentanyl was discovered in 1960.[71]

---

67 Van Ree, Jan M. et al., "Opioids, Reward and Addiction: An Encounter of Biology, Psychology, and Medicine," *Pharmacological Reviews*, 51:2, 1999, p. 344.

68 "Opioids," The Merck Manual for Healthcare Professionals, July 2008, http://www merck.com/mmpe/sec15/ch198/ch198f html#sec15-ch198-ch198l-384p.

69 Miro, Oscar et al., "Morphine in acute heart failure: good in relieving symptoms, bad in improving outcomes," *Journal of Thoracic Disease*, 9:9, 2017, pp. E871-E874.

70 "History of Heroin," United Nations Office on Drugs and Crime, https://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1953-01-01_2_page004 html.

71 Crow, James M., "Addicted to the Cure," *Chemistry World*, January 3, 2017, The Royal Society of Chemistry, https://www.chemistryworld.com/features/new-opioid-drugs/2500163.article; Murray, Alison and Neil Hagen, "Hydromorphone," *Journal of Pain and Symptom Management*, 29:5S, May 2005, p. S57; Wong, Thomas, "Hydrocodone extended-release," in *The Essence of Analgesia*

46. The 1960s and 1970s saw approval of several short-acting combination products. These included Percocet (oxycodone / acetaminophen), approved in 1976, and Vicodin (acetaminophen / hydrocodone), approved in 1978.[72] In the late 1980s and early 1990s, the U.S. Food and Drug Administration ("FDA") approved long-acting formulations of opioids for the treatment of chronic pain, such as MS Contin (morphine) in 1987 and OxyContin (oxycodone) in 1995. At the time of the approval of these products, the FDA believed there would be less abuse potential with LAOs since the drug would be absorbed slowly without an immediate rush or "high."[73]

47. In the last decade, several opioid products were altered to make them less susceptible to abuse.[74] These reformulations are known as abuse deterrent formulations ("ADFs"). In some products, pills were altered to prevent chewing, crushing, or cutting, all of which limit patients from circumventing the extended release systems used in the pills.[75] In other products, opioids are combined with agonists or antagonists, such as naltrexone or naloxone, in order to reduce or remove the euphoric feeling associated with abuse.[76]

---

and Analgesics (Raymond Sinatra, Jonathan Jahr and J. Michael Watkins-Pitchford Eds.), Cambridge University Press, 2011, p. 452.

72 "FDA Approved Products," Drugs@FDA, NDA: 085106, https://www.accessdata fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=085106; "Glossary of Terms," John Hopkins Medicine, https://www hopkinsmedicine.org/news/articles/glossary-of-terms.

73 "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," FDA, https://www fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf.

74 "Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling," FDA, April 2015, https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf, p. 2. See also Becker, William C. and David A. Fiellin, "Abuse-Deterrent Opioid Formulations — Putting the Potential Benefits into Perspective," *New England Journal of Medicine*, 376: 22, 2017, p. 2104.

75 Products include Arymo ER (morphine), Hysingla ER (hydrocodone), MorphaBond ER (morphine), OxyContin (oxycodone), and RoxyBond (oxycodone) (Loeser, Kathryn C. and Ryan Rodriguez, "Regulatory and evidence-based considerations for abuse-deterrent opioids," *American Journal of Health-System Pharmacy*, 76:2, ("Loeser and Rodriquez"), pp. 114-118).

76 Embeda (morphine–naltrexone) is currently marketed as an ADF. Targiniq ER (oxycodone–naloxone) and Troxyca ER (oxycodone–naltrexone) were approved by the FDA but have since been discontinued (Loeser and Rodriquez, p. 115).

(c) Opioid Utilization

48. The ten most commonly prescribed opioids in the U.S. for 2001, 2006, 2011, and 2016 are shown in Exhibit III-2.[77] Prescribing between 2011 and 2016 declined for almost all of the top ten with little change in the relative rankings. Nationally, MME prescribed declined by 20 percent from 2011 to 2016. Exhibits III-3 and III-4 indicate the most commonly prescribed opioids by MME in the Counties. MME utilization in Cuyahoga Country declined by 29 percent from 2011 to 2016; MME utilization in Summit Country declined by 45 percent from 2011 to 2016.

49. Exhibit III-5 shows opioid prescriptions in MME written per 100 persons at the national level and in the Counties between 1997 and 2017. The opioid prescribing rate in the U.S. and in the Counties rose between 1997 and 2010, but then declined through 2017.

C. Prescribing Guidelines

50. Clinical practice guidelines are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."[78] For many medical conditions, clinical guidelines have been developed to define "best practices" for the diagnosis and treatment of patients.[79] Typically developed by professional societies or government agencies, these guidelines tend to be publicly available and widely disseminated in the medical community;[80] they often become part of continuing medical education

---

77 The exhibit is based on data from IQVIA, a standard data source for the pharmaceutical industry.

78 Field, Marilyn J. and Kathleen N. Lohr, eds., "Guidelines for Clinical Practice: From Development to Use," *Institute of Medicine*, 1992, p. 2.

79 Graham, Robin et al., "Clinical Practice Guidelines We Can Trust," *Institute of Medicine*, 2011, p. 13.

80 See, for example, National Guidelines Clearinghouse at www.guideline.gov and Institute for Clinical Systems Improvement at www.icsi.org.

curricula. Guidelines do not exist to replace clinical judgement.[81] Accordingly, clinicians' adherence to guidelines is not mandatory.[82]

51. Several organizations have developed clinical practice guidelines for the treatment of pain.[83] With respect to opioids specifically, guidelines aim to "improve communication between clinicians and their patients about the risks and benefits of opioid therapy."[84] Opioid use guidelines that are particularly relevant include those that contain information with respect to the treatment of chronic pain, cancer pain, and acute pain (including post-operative pain). Below, I discuss each of these types of guidelines, in turn. In addition, certain guidelines have changed over time, motivating changes in prescribing behavior, as discussed later in this report.

(a) Chronic Pain

52. Examples of opioid prescribing guidelines for the treatment of chronic pain are available from several sources, including the Department of Veterans Affairs ("VA") in conjunction with the Department of Defense ("DOD") in 2003, 2010, and 2017 ("VA/DOD Guidelines");[85] the Centers for Disease Control and Prevention ("CDC") in 2016 ("CDC Guidelines");[86] American Academy of

---

81 Dowell, Deborah, Tamara M. Haegerich, and Roger Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016," *JAMA*, 315:15, 2016, ("Dowell et al. 2016"), p. 1625.

82 Schneider, Jennifer, P., Gary W. Jay, Leonard Goldstein, and Elmer G. Pinzon, "CDC Issues Final Guidelines for Opioid Prescribing: PPM Editorial Board Responds," *Practical Pain Management*, 6:3, 2018, p. 1.

83 Barth, Kelly S., Constance Guille, Jenna McCauley, and Kathleen T. Brady, "Targeting practitioners: A review of guidelines, training, and policy in pain management," *Drug and Alcohol Dependence*, 173, 2017, ("Barth et al. 2017"), p. 2.

84 Dowell et al. 2016, p. 1625.

85 "Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain," VA and DOD, 2003, ("VA/DoD 2003"), pp. 2-31; "Management of Opioid Therapy for Chronic Pain," VA and DOD, 2010, ("VA/DoD 2010"), pp. 3-73; "Clinical Practice Guideline for Opioid Therapy for Chronic Pain," VA and DOD, 2017, ("VA/DoD 2017"), pp. 3-198.

86 Dowell et al. 2016, pp. 1624-1645.

Family Physicians ("AAFP Guideline");[87] and state of Ohio in 2018 ("Ohio Guidelines").[88]

53. Guidelines on the treatment of chronic pain tend to recommend that prescribers conduct a risk assessment prior to the decision to prescribe (or renew a prescription for) opioids to a patient.[89] The purpose of this assessment is to determine a patient's risk of opioid misuse, abuse, or addiction.[90] For each patient, prescribers are advised to weigh the benefits of prescription opioids against the potential costs.[91] Furthermore, some guidelines explicitly state that, as a part of any risk assessment, prescribers should consider the possibility of non-opioid alternative treatments; that is, prescribers should consider if any benefits provided by opioids are in excess of the benefits of non-opioid treatments, prior to prescribing opioids.[92] As such, the guidelines advise physicians regarding the inherent risks of opioid prescribing and the related importance of communication with the patient.[93]

---

87 Lembke, Anna, Keith Humphreys and Joran Newmark, "Weighing the Risks and Benefits of Chronic Opioid Therapy," *American Family Physician*, 93:12, 2016, ("Lembke et al. 2016"), pp. 982-990.

88 "New Rules for Chronic Pain Prescriptions will help patients and prescribers work to prevent addition," State of Ohio Communication, May 2, 2018, ("Ohio State Medical Board 2018").

89 For example, the CDC Guidelines recommend that clinicians consider factors such as a history of overdose, a history of substance use disorder, and higher opioid dosages as factors that could increase a patient's risk of opioid misuse or abuse (Dowell et al. 2016, pp. 1638-1639). The VA/DoD Guidelines (2003, 2010) recommend that opioid therapy should be used only after careful consideration of the risks and benefits to the patient (see, for example, VA/DoD 2003, p. 8; VA/DoD 2010, p. 15).

90 Chou, Roger et al., "Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain," *Journal of Pain*, 10:2, p. 116.

91 See Dowell et al. 2016, p. 1633.

92 For example, the VA/DoD Guidelines of 2017 recommend against the initiation of long-term opioid therapy in general (VA/DoD 2017, p. 7). Both the CDC Guidelines and Ohio Guidelines suggest that prescribers first consider non-pharmacologic and non-opioid therapies (Dowell et al. 2016, p. 1633; Ohio State Medical Board 2018, p. 1).

93 For example, the CDC Guidelines state that the risk and benefits of opioid therapy should be reviewed with the patient prior to initiating treatment (Dowell et al. 2016, p. 16). The VA/DoD Guidelines (2010, 2017) advise clinicians to discuss with the patient the "risks and benefits of opioid therapy" (VA/DoD 2010, p. 16; VA/DoD 2017, p. 51). The AAFP Guideline recommends that physicians take sufficient time to educate patients in "simple language" on the associated risks of initiating opioid therapy (Lembke et al. 2016, p. 984). The Ohio Guidelines require physicians to engage in conversations with patients before starting them on long-term opioid treatment (Ohio State Medical Board 2018, p. 1).

54. The CDC Guidelines recommend that prescribers use state Prescription Drug Monitoring Program ("PDMP") data to see if patients are currently taking any other drugs that, in combination with opioids, put them at a higher risk for overdose.[94] Additionally, prescribers are advised to use PDMP data to determine whether patients are currently taking or have received any other opioid medication from other prescribers (also known as "doctor shopping").[95]

55. Once the decision to prescribe opioids has been made, a common recommendation is that opioid prescriptions start off at a "low" dose. For example, the CDC Guidelines state that when starting opioids for chronic pain, the "lowest effective dosage" should be prescribed and it should only be "increased by the smallest practical amount."[96] The AAFP Guideline suggests that physicians "procced with caution" by prescribing the "lowest possible dose for the shortest duration."[97]

56. Dosages considered "low" or "high" vary by guideline and have changed over time. For example, the VA/DoD Guidelines from 2010 suggested a maximum dosage of 200 MME per day;[98] the VA/DoD Guidelines from 2017 consider "low" dosages to be 20 MME per day and recommend against dosages over 90 MME per day for treating chronic pain.[99]

57. Guidelines have become more stringent over time with regards to the choice between short-acting and long-acting opioids. Earlier VA/DoD Guidelines (2003, 2010) recommended the use of LAOs for patients with continuous pain and short-acting opioids for patients with intermittent pain.[100] In contrast, the CDC Guidelines recommend that when initiating opioid therapy, clinicians should

---

94 Dowell et al. 2016, p. 1639.
95 Dowell et al. 2016, p. 1640.
96 Dowell et al. 2016, p. 1637.
97 Lembke et al. 2016, p. 984.
98 VA/DoD 2010, p. 29.
99 VA/DoD 2017, pp. 8, Appendix D Drug Tables.
100 VA/DoD 2003, pp. 12-13; VA/DoD 2010, p. 26.

prescribe short-acting opioids instead of LAOs.[101] The VA/DoD Guidelines from 2017 also recommend against the use of LAOs when initiating treatment for chronic pain patients.[102] Furthermore, the VA/DoD Guidelines from 2017 recommend that LAOs be reserved for patients for whom alternative analgesic treatments (e.g. non-opioid analgesics or short-acting opioids) are ineffective or inadequate.[103]

58. Regarding treatment durations, the CDC Guidelines and the VA/DoD Guidelines from 2017 recommend a short duration of treatment and suggest that therapy for chronic pain beyond 90 days requires re-evaluation.[104] Prescribers are recommended to follow up with their patients at least once every six months and preferably more frequently.[105] At these follow-up meetings, prescribers should examine their patients for any sign of opioid dependence.[106]

59. After following up with the patient, prescribers must decide if a change in dosage (or discontinuation) is warranted. Effectively, guidelines recommend prescribers conduct a new risk assessment at each follow-up visit. If the prescriber determines that the risks of the prescription opioids are exceeding the benefits (or lack thereof), then the prescriber should consider either lowering the dosage or discontinuing the patient off opioids entirely.[107] The AAFP Guideline

---

101 Dowell et al. 2016, p. 1637.

102 VA/DoD 2017, p. 54.

103 VA/DoD 2017, p. 90.

104 See Dowell et al. 2016, p. 1638 and VA/DoD 2017, p. 40. The VA/DoD Guidelines (2003, 2010) do not recommend optimal treatment duration.

105 For example, the CDC Guidelines recommend that physicians monitor patients within 1 to 4 weeks of starting opioid therapy and following that at least once every 3 months (Dowell et al. 2016, p. 1638). The AAFP Guideline recommends that physicians re-evaluate patients "at least every three months, even when stable and doing well, and more frequently if problems arise" (Lembke et al. 2016, p. 984).

106 Dowell et al. 2016, p. 1639; VA/DoD 2017, pp. 11, 14.

107 For example, the CDC Guidelines recommend going to a lower dosage or discontinuation if a patient is treated with more than 90 MME of opioid per day (Dowell et al. 2016, p. 1637). See also VA/DoD 2017, p. 63.

recommends against "abruptly" discontinuing opioid therapy in case doing so induces acute opioid withdrawal.[108]

60. In some cases, prescribers might determine that an increase in dosage is required. In these instances, guidelines suggest that if certain dosage thresholds are exceeded, then additional or more frequent monitoring requirements should be implemented. For example, the CDC Guidelines recommend that if a dosage increases above 50 MME per day, prescribers should increase their frequency of follow-ups and evaluate whether patients are progressing appropriately.[109] The Ohio Guidelines state that if dosages exceed 50 MME per day, clinicians should re-evaluate the status of the patient's underlying condition causing pain, assess functioning, look for signs of prescription misuse or abuse, consider consultation with a specialist, and obtain written informed consent. Additional patient re-evaluation thresholds in the Ohio Guidelines occur at 80 MME per day and 120 MME per day.[110]

61. Finally, as with the initial prescription decision, the CDC Guidelines recommend that clinicians review PDMP data throughout the course of therapy to help determine if the patient is using the opioid as prescribed or if there are any dangerous combinations that may put the patient at a high risk for overdose.[111] Similarly, the AAFP Guideline recommends that prescribers use PDMP data to check for evidence of early refills or total MMEs exceeding 120 mg per day.[112]

(b) Cancer Pain

62. Prescribing guidelines for the treatment of cancer pain are available from the National Comprehensive Cancer Network ("NCCN"; "NCCN Guidelines")[113] and

---

108 Lembke et al. 2016, p. 984.

109 Dowell et al. 2016, p. 1638.

110 Ohio State Medical Board 2018, pp. 1-2.

111 Dowell et al. 2016, p. 1638.

112 Lembke et al. 2016, p. 984.

113 Swarm, Robert A. et al., "NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain," NCCN, 2016, ("Swarm et al. 2016"), pp. Update Page 1-M-43.

the American Society of Clinical Oncology ("ASCO"; "ASCO Guidelines").[114] Individual cancer care centers have also issued guidelines, such as the University of Texas MD Anderson Cancer Center ("MD Anderson Guidelines"). The Cleveland Clinic Foundation also has published a selection of recommended strategies for opioid administration in cancer pain management ("Cleveland Clinic Guidelines").[115]

63. The previously noted WHO Pain Ladder emerged in 1986 with guidance on the management of cancer pain.[116] The guidance has maintained that "pharmacological treatment is the mainstay of cancer pain management."[117] The WHO Pain Ladder states that in the case of patient pain: "[T]here should be prompt oral administration of drugs in the following order: non-opioids (aspirin and paracetamol [i.e., acetaminophen]); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain."[118] Relatedly, a policy statement from ASCO highlights that "cancer patients should be largely exempt from regulations restricting access to or limiting doses of prescription opioids in recognition of the unique nature of their disease, its treatment, and potentially life-long adverse health effects from having had cancer."[119]

64. The NCCN Guidelines recommend pain management strategies based on a Pain Intensity Rating (or "pain score"), where "Mild," "Moderate," and "Severe" are defined with pain scores of 0-3, 4-6, and 7-10, respectively.[120] The NCCN

---

114 Paice, Judith A. et al., "Management of Chronic Pain in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline," *Journal of Clinical Oncology*, 34:27, 2016, ("Paice et al. 2016"), pp. 3325-3345.

115 Bruera, Eduardo et al., "Cancer Pain: Adults," MD Anderson Cancer Center, 2017, ("Bruera et al. 2017"), pp. 1-23; Walsh, Declan et al., "Strategies for Pain Management: Cleveland Clinic Foundation Guidelines for Opioid Dosing for Cancer Pain," *Supportive Cancer Therapy*, 1:3, 2004, ("Walsh et al. 2004"), pp. 157- 164.

116 "Cancer pain relief and palliative care," WHO, 1986, p. 12.

117 "Cancer pain relief and palliative care," WHO, 1990, p. 7.

118 "WHO's cancer pain ladder for adults," WHO, https://www.who.int/cancer/palliative/painladder/en/.

119 "ASCO Opioids Toolkit," ASCO, 2016.

120 Swarm et al. 2016, p. PAIN-3.

Guidelines recommend opioids for patients with a pain score of 4 or above.[121] The MD Anderson Guidelines use patient pain score assessments, similar to those recommended by the NCCN Guidelines, to identify if patients should be prescribed opioids or not.[122] The MD Anderson Guidelines also recommend that the physician discuss with patients the "desired level/intensity of pain that will allow the patient to achieve comfort" (termed "Personalized Pain Goal" or "PPG").[123]

65. The ASCO Guidelines make recommendations for adult patients "diagnosed with cancer and … experiencing pain that lasts [at least] 3 months, irrespective of cause."[124] The ASCO Guidelines recommend that clinicians prescribe non-opioid analgesics but "may prescribe a trial of opioids in carefully selected cancer survivors with chronic pain who do not respond to more conservative management and who continue to experience pain-related distress or functional impairment."[125]

66. The Cleveland Clinic Guidelines recommend that "[o]pioid dosing should be adapted to the individual needs" of the patient and that [a]ppropriate doses are established by titration based upon individual analgesic response and side effects, rather than age, gender, or ethnicity."[126]

67. When initiating long-term opioid treatment, ASCO Guidelines recommend that clinicians assess the potential risks and benefits, provide education to patients and their families regarding the risks, and dispel misconceptions regarding opioid use.[127] Similarly, the NCCN Guidelines recommend that upon treatment initiation, prescribers should conduct a patient risk assessment, educate patients

121 Swarm et al. 2016, p. MS-7.
122 Bruera et al. 2017, p. 5.
123 Bruera et al. 2017, pp. 2, 5.
124 Paice et al. 2016, p. 3326.
125 Paice et al. 2016, p. 3327.
126 Walsh et al. 2004, p. 158.
127 Paice et al. 2016, p. 3340.

on the risks associated with opioids, and provide additional support services and education to "high-risk (of opioid abuse) patients."[128] If patients begin to exhibit aberrant behaviors, the ASCO Guidelines recommend a reevaluation of the opioid prescribing decision.[129] If, in this situation, prescribers still feel that the benefits of prescribing opioids outweigh the costs, the ASCO Guidelines recommend increased or restructured precautions to increase control and adherence monitoring.[130] Similarly, the NCCN Guidelines recommend that if "signs of aberrant opioid use are present, providers should consider limiting or restricting use to avoid risk of diversion."[131] Potential precautionary methods recommended by the ASCO Guidelines include avoiding agents with higher abuse potential, prescribing small amounts at short intervals, routine reviewing of PDMP data and monitoring the use of substances through urine or other toxicology screening.[132]

68. The Cleveland Clinic Guidelines recommend extended-release opioids for long-term pain management.[133] For patients with a history of substance abuse, the Cleveland Clinic Guidelines recommend that opioid prescriptions be accompanied by "[f]requent visits and small prescriptions combined with accountability through pain contracts."[134]

(c) Acute Pain

69. The CDC Guidelines recognize that "long-term opioid use often begins with treatment of acute pain."[135] Consequently, the CDC Guidelines recommend that for "pain severe enough to require opioids," clinicians should prescribe the "lowest effective dose of immediate-release opioids."[136] The CDC Guidelines

128 Swarm et al. 2016, p. PAIN-E
129 Paice et al. 2016, p. 3337.
130 Paice et al. 2016, p. 3337.
131 Swarm et al. 2016, p. MS-16
132 Paice et al. 2016, p. 3337.
133 Walsh et al. 2004, p. 162.
134 Walsh et al. 2004, p. 163.
135 Dowell et al. 2016, p. 1638.
136 Dowell et al. 2016, p. 1638.

state that a three day supply of opioids should be "sufficient," and that a supply of over seven days will "rarely be needed."[137]

70. I understand that in Ohio, a seven day supply limit per initial prescription of opioids for adults with acute pain was mandated by legislation in 2017. In addition, the prescription could not exceed an average of 30 MME per day. Limits are permitted to be exceeded if the duration of pain is expected to be longer than the seven-day limit. In these cases, the rationale must be documented to include why a non-opioid was not sufficient.[138]

71. Generally, prescribing recommendations for acute pain are provided by specialty guidelines associated with specific forms of acute pain. The CDC Guidelines suggest that while some recommendations related to chronic pain may be relevant for the management of acute pain, clinicians should refer elsewhere for prescription guidance within acute care settings.[139] Examples of guidelines discussing acute pain management include the following.

(a) The VA/DoD published guidelines for the management of postoperative pain ("VA/DoD Postoperative Pain Guidelines") in 2002. These guidelines state: "Opioid agents are the mainstay of postoperative analgesia … pain management with these agents should be individually tailored to patient response. There is no ceiling dose for pure agonist opioids."[140] The VA/DoD Postoperative Pain Guidelines describe dosage and administration route recommendations by associated opioid product.[141] For example, when prescribing oxycodone orally, the Guidelines recommend an initial dose of 5-15 mg every 4-6 hours;[142]

137 Dowell et al. 2016, p. 1638.

138 CCF000058 at 080-81; "New Limits on Prescription Opioids for Acute Pain," Ohio SMB, https://med.ohio.gov/Portals/0/Resources/Prescriber%20Resources/AcuteRulesHandout.pdf.

139 Dowell et al. 2016, p. 1625.

140 "Clinical Practice Guideline for the Management of Postoperative Pain: Options for Postoperative Pain Management: Pharmacologic Management," VA and DoD 2002, pp. 1-81, ("VA/DoD 2002") p. 9.

141 VA/DoD 2002, pp.19 – 41.

142 VA/DoD 2002, p. 24.

when prescribing fentanyl intra-muscularly, the Guidelines recommend 25-100 micrograms as needed.[143]

(b) In 2018, Johns Hopkins University issued Opioid-Prescribing Guidelines for Common Surgical Procedures ("Johns Hopkins Guidelines"), which are based on prescriber and patient consensus prescription recommendations for specific, common surgical procedures.[144] Physicians are recommended to prescribe non-opioid medications where possible. The recommended maximum daily opioid dosage prescribed at discharge for any of the studied common surgeries should not exceed 150 MME.[145]

D. Benefits of Opioid Treatment

72. A large literature examines the short-term efficacy of opioids for the treatment of chronic pain.[146] Several meta-analyses attempt to characterize the main findings of this literature, generally finding that opioids have a positive and statistically significant effect on reducing pain.[147] There also exist studies that examine the effectiveness of opioids compared to non-opioid pain medications. These studies

---

143 VA/DoD 2002, p. 26.

144 Overton, Heidi N. et al., "Opioid-Prescribing Guidelines for Common Surgical Procedures: An Expert Panel Consensus," *Journal of American College of Surgeons*, 277:4, 2018, ("Overton et al. 2018"), pp. 411-418.

145 Overton et al. 2018, p. 416. See also "Calculating Total Daily Dose Of Opioids For Safer Dosage," CDC, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf.

146 See, for example, Dowell, Deborah et al., "CDC Guideline for Prescribing Opioids for Chronic Pain —United States, 2016," Morbidity and Mortality Weekly Report, 65:1, 2016, ("Dowell et al. 2016"), p. 2; Furlan, Andrea D. et al., "Opioids for Chronic Noncancer Pain: a Meta-analysis of Effectiveness and Side Effects," *Canadian Medical Association Journal*, 174:11, 2006, p.1589; Chou, Roger, et al., "The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop," *Annals of Internal Medicine*, 162, 2015, ("Chou et al. 2015"), p. 276.

147 See, for example, Furlan, Andrea D. et al., "A comparison between enriched and non-enriched enrollment randomized withdrawal trials of opioids for chronic noncancer pain," *Pain Research and Management*, 16:5, 2011, ("Furlan et al. 2011"), pp. 346-347; Dowell et al. 2016, p. 2; Busse, Jason W. et al., "Opioids for Chronic Noncancer Pain A Systematic Review and Meta-analysis," *Journal American Medical Association*, 320:23, 2018, ("Busse et al. 2018"), p. 2451. For examples of discrepancies among meta-analyses and studies regarding opioid use for chronic pain, see Chou et al. 2015, pp. 276-277; Dowell et al. 2016, p. 9; Busse et al. 2018, pp. 2449-2450.

find in general that "stronger" opioids (e.g., oxycodone and morphine) lead to statistically significant reductions in pain.[148]

73. Following the implementation of the CDC Guidelines, government payors such as Medicaid programs and the VA have sought to limit MME levels prescribed for chronic pain; some commercial payors may have followed suit. It is suggested, however, that the result has been the "pendulum swinging too far," causing harm to chronic pain patients due to untreated pain.[149] Physicians have reported patients who have suffered as a result,[150] and a group of practitioners has called for less harmful practices in tapering opioid doses among long-term patients.[151] The authors of the CDC guidelines have recently opined that some policies and practices purportedly from the guidelines "have in fact been inconsistent with, and often go beyond, its recommendations," including discontinuation for patients receiving high doses.[152] Individuals with chronic pain who had opioids taken away from them have been found to have experienced an increase in suicidal tendencies,[153] and in some cases attempted to take their own lives.[154]

74. Half of all cancer patients, especially those with advanced stages, will suffer from moderate to severe pain.[155] As discussed above, the WHO has long recognized

---

148 See, for example, Rosenblum, Andrew et al., "Opioids and the Treatment of Chronic Pain: Controversies, Current Status, and Future Directions," *Experimental and Clinical Psychopharmacology*, 16:5, 2008, p. 10; Furlan et al. 2011, p. 347.

149 Schatman, Michael E. et al., "Opioid moderatism and the imperative of rapprochement in pain medicine," *Journal of Pain Research*, 12, 2019, ("Schatman et al. 2019"), pp. 651-652.

150 Glod, Susan A., "The Other Victims of the Opioid Epidemic," *New England Journal of Medicine*, 376:22, 2017, pp. 2101-2102.

151 Darnall, Beth D. et al., "International Stakeholder Community of Pain Experts and Leaders Call for an Urgent Action on Forced Opioid Tapering," *Pain Medicine*, 20, 2019, pp. 429-433.

152 Dowell, Deboarah et al., "No Shortcuts for Safer Opioid Prescribing, *New England Journal of Medicine*, April 24, 2019.

153 Demidenko, Michael I. et al., "Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users," *General Hospital Psychiatry*, 47, 2017, pp. 32-34.

154 Szalavitz, Maia, "When the Cure Is Worse Than the Disease," *The New York Times*, February 9, 2019.

155 Wiffen, Phillip J. et al., "Opioids for cancer pain - an overview of Cochrane reviews," *Cochrane Database of Systematic Reviews*, 7, 2017, ("Wiffen et al. 2017), p. 3; Caraceni, Augusto, et al, "Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC," *Lancet Oncology*, 13, 2012, ("Caraceni et al. 2012") p. e58; Reid, Colette M, et al.,

opioids as an important and effective option in treating cancer pain.[156] Studies find that at least 80 percent of cancer patients treated with opioid therapies realize adequate pain relief.[157]

75. Breakthrough cancer pain ("BTCP") is a significant complication in the treatment of cancer pain. BTCP is a type of acute pain that occurs suddenly during cancer treatment.[158] Meta-analyses indicate that short-acting opioids are effective in relieving breakthrough cancer pain and that fentanyl may be more effective for this pain than other opioids.[159]

E. Oversight of Opioids: Federal

76. I understand that the manufacturing and distribution of prescription opioids are governed by a complex and interlinked system of regulatory oversight, occurring at the federal and state levels. At the federal level, important regulatory functions are performed by the FDA and the DEA.

(a) FDA

77. The FDA is responsible for assuring the safety and efficacy of pharmaceuticals used to treat humans.[160] The FDA evaluates applications for marketing approval of branded drugs (including prescription opioids) on the basis of clinical trial data

---

"Oxycodone for Cancer-Related Pain: Meta-analysis of Randomized Controlled Trials," *Archives of Internal Medicine*, 166, 2006, ("Reid et al. 2006"), p. 837; Trescott, Andrea M, "Review of the Role of Opioids in Cancer Pain," *Journal of the National Comprehensive Cancer Network*, 8:9, 2010, p. 1087.

156 Caraceni et al. 2012, p. e58; "WHO's cancer pain ladder for adults," WHO, https://www.who.int/cancer/palliative/painladder/en/ ("WHO's cancer pain ladder for adults").

157 Wiffen et al. 2017, p. 15; Jandhyala, Ravi et al., "Efficacy of Rapid-Onset Oral Fentanyl Formulations vs. Oral Morphine for Cancer-Related Breakthrough Pain: A Meta-Analysis of Comparative Trials," *Journal of Pain and Symptom Management*, 46:4, 2013, ("Jandhyala et al. 2013") p. 574.

158 Jandhyala et al. 2013, p. 574.

159 Reid et al. 2006, p. 837; Caraceni et al. 2012, p. e59; Hanks, GW et al., "Morphine and alternative opioids in cancer pain: the EAPC recommendations," *The British Journal of Cancer*, 84:5, 2001 ("Hanks et al. 2001"), p. 587.

160 Barth, Kelly S. et al., "Targeting practitioners: A review of guidelines, training, and policy in pain management," *Drug and Alcohol Dependence*, 173, 2017, ("Barth et al. 2017"), p. 12.

on safety and efficacy collected during the drug development process.[161] Once approval is obtained, the FDA ensures that the information disclosed on the product's label is consistent with available scientific evidence. All claims made by the company in marketing the product must be consistent with the labeling approved by the FDA.[162] In addition, the FDA has the authority to request post-marketing approval studies, which can contribute to the monitoring of the safety and efficacy of products over time.[163]

78. Exceptions to FDA approval based on safety or efficacy evidence were provided through "grandfathering" provisions, which enabled any product approved before 1962 to be marketed. These provisions applied to some opioids, such as morphine products, methadone products, and certain hydrocodone combination products (hydrocodone/ guaifenesin and hydrocodone/ pseudoephedrine).[164] Since 2006, the FDA has required unapproved products to be evaluated and approved, or else withdrawn from the market, with some discretion exercised.[165]

79. With respect to labeling prescription opioids, OxyContin's original label in 1995 contained a safety warning advising against "break[ing], chew[ing,] or crush[ing]" the tablets because doing so "could lead to the rapid release and

---

161 With respect to generic drugs, there is an abbreviated process that does not typically depend on the applicant providing additional clinical trial evidence ("Abbreviated New Drug Application (ANDA)," FDA, https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/default.htm).

162 21 CFR 201.56 (a) (1-3) (2019).

163 Fain, K. et al., "The Food and Drug Administration Amendments Act and Postmarketing Commitments," *JAMA Network*, 310:2, 2013, p. 202; "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," National Academies of Sciences, Engineering, and Medicine, 2017 ("Pain Management and Opioid Epidemic Report 2017"), p. 371.

164 "Marketed Drugs That Have Not Received FDA Approval," RADARS System, Quarter 4, 2008, https://www.radars.org/system/publications/2008Q4-RADARS-System-Newsletter.pdf.

165 Gupta, Ravi et al., "The FDA Unapproved Drugs Initiative: An Observational Study of the Consequences for Drug Prices and Shortages in the United States," *Academy of Managed Care Pharmacy,* 23:10, 2017, p. 1067; "Guidance for FDA Staff and Industry: Marketed Unapproved Drugs—Compliance Policy Guide," FDA, September 2011, https://www.fda.gov/media/71004/download, p. 2.

absorption of a potentially toxic amount of oxycodone."[166] In 2001, the FDA required a "Black Box" warning on OxyContin's label, the highest level of warning on a product label.[167] The "Black Box" warning noted that taking OxyContin in the manner described above "leads to rapid release and absorption of a potentially fatal dose of oxycodone."[168] In addition, in 2001, label information related to the incidence of addiction was also revised. In 1995, the label stated that "delayed absorption as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug."[169] In 2001, the language was updated to emphasize that there were insufficient data to "establish the true incidence of addiction in chronic patients."[170] Finally, the FDA required that the description of the appropriate duration for which OxyContin should be prescribed be updated in 2001. In 1995, the label stated that OxyContin should be prescribed "where use of an opioid analgesic is appropriate for more than a few days."[171] In 2001, the approved label added that the product be prescribed "when a continuous, around-the-clock analgesic is needed for an extended period of time."[172]

80. In 2013, the FDA announced labelling changes for extended-release/long-acting opioid labeling (ER/LA), including additional precautionary warnings, indication details, and safety information.[173] For example, this new labelling required that

166 "OxyContin Abuse and Diversion and Efforts to Address the Problem," GAO, December 2003, https://www.gao.gov/new.items/d04110.pdf, ("GAO Report 2003"), p. 35.

167 GAO Report 2003, p. 34.

168 GAO Report 2003, p. 35. A possible unintended consequence of this warning was that it effectively doubled as an instruction manual for how OxyContin could be used for illicit purposes (Jayawant, Sujita S. and Rajesh Balkrishnan, "The Controversy Surrounding OxyContin Abuse: issues and solutions," *Therapeutics and Clinical Risk Management*, 1:22, 2005, p. 80).

169 GAO Report 2003, p. 34; "How Oxycodone Has Contributed to the Opioid Epidemic," Pharmacy Times, August 2018, https://www.pharmacytimes.com/contributor/marilyn-bulloch-pharmd-bcps/2018/08/how-oxycodone-has-contributed-to-the-opioid-epidemic.

170 GAO Report 2003, p. 34.

171 GAO Report 2003, p. 35.

172 GAO Report 2003, p. 35.

173 Letter from Bob A. Rappaport, Center for Drug Evaluation and Research, to ER/LA Opioid Application Holders, September 10, 2013, https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM367697.pdf, ("Rappaport Letter 2013"). Previous labelling specified that ER/LA opioids are indicated for patients whose pain is "moderate-to-severe pain when a continuous, around-the clock analgesic is needed for an extended period of time." By

ER/LA opioids be indicated for the "management of pain severe enough to require daily, around-the clock, long-term opioid treatment and for which alternative treatment options are inadequate."[174] Previously, ER/LA opioid labels indicated use for moderate to severe pain patients, on an "as-needed" basis.[175] Additional safety warnings regarding chronic maternal use during pregnancy and the risks of "life-threatening neonatal opioid withdrawal syndrome" are also mandated by the FDA label changes.[176] In February 2019, the FDA announced that it would require all manufacturers of current and future prescription opioids (except short-acting treatments, including those for hospital use) to conduct clinical trials to determine whether opioids are effective in the treatment of chronic pain.[177]

81. In 2013, the FDA also published draft guidance designed to "incentivize the development of safer, less abusable opioid analgesics, and … facilitate the dissemination of fair and accurate information regarding such products."[178] Specifically, the FDA provided manufacturers with information on how "abuse-deterrent properties of opioid analgesic products should be studied and evaluated,

---

comparison, the 2013 update requires that ER/LA opioids are indicated for pain "severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatments to manage the pain are inadequate." (Barlas, Stephen, "FDA Requires new labelling for some opioids: Modest changes walk narrow political line," *Pharmacy and Therapeutics*, 38:11, 2013 ("Barlas 2013"), p. 644).

174 Rappaport Letter 2013.

175 "FDA makes labelling changes for opioid painkillers," National Pain Report, http://nationalpainreport.com/fda-makes-labeling-changes-opioid-painkillers-8821614.html, ("National Pain Report").

176 Rappaport Letter 2013.

177 See, for example, Bernstein, Lenny and Laurie McGinley, "FDA takes fresh look at whether opioids are effective for chronic pain," *Washington Post*, February 25, 2019, https://www.washingtonpost.com/national/health-science/fda-takes-fresh-look-at-whether-opioids-are-effective-for-chronic-pain/2019/02/25/227a5fe6-3917-11e9-a06c-3ec8ed509d15_story.html?noredirect=on&utm_term=.bea32b785be8; Dyer, Owen, "US opioid epidemic: FDA demands studies of whether opioids do control chronic pain," *British Medical Journal*, 364:959, 2019, p. 364.

178 78 FR 2676 (January 14, 2013).

and what claims regarding such properties may be suitable for inclusion in labeling."[179]

82. In 2016, leadership within the FDA called for an action plan to "reassess the agency's approach to opioid medicines."[180] The FDA Opioids Action Plan ("OAP") introduced initiatives targeting the growth of opioid misuse while also seeking to ensure patient access to pain relief. Key elements of this plan are summarized below.

(a) **Expanding the use of advisory committees.** The FDA relies on committees and panels to obtain "independent, expert advice on scientific, technical and policy matters."[181] As the committees act in an advisory capacity, recommendations are not binding and the FDA is not required to implement them.[182] Per the OAP, the FDA committed to convening an expert advisory committee before approving any new opioid marketing approval application that does not have abuse-deterrent properties as well as establishing and consulting a Pediatric Advisory Committee regarding a framework for pediatric opioid labeling.[183]

(b) **Improving product labelling.** The FDA committed to developing updates to immediate-release opioid labeling, including "additional warnings and safety information that incorporate elements similar to the extended-release/long-acting (ER/LA) opioid analgesics."[184]

---

179 78 FR 2676 (January 14, 2013).

180 "Califf, FDA top officials call for sweeping review of agency opioids policies," FDA News Release, February 4, 2016, https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm484765.htm, ("FDA Review Opioid Policies 2016").

181 "Advisory Committees," FDA, https://www.fda.gov/AdvisoryCommittees/default.htm.

182 For example, there are cases where the FDA approves products despite contrary advice; e.g. in 2013, Zohydro ER, was approved by the FDA despite an advisory committee of pain specialists voting 11-2 against the approval ("Pure Hydrocodone, Stronger than Vicodin, Approved by FDA," CBS News article, https://www.cbsnews.com/news/pure-hydrocodone-stronger-than-vicodin-approved-by-fda/).

183 FDA Review Opioid Policies 2016.

184 FDA Review Opioid Policies 2016.

(c) **Strengthening post-market requirements and risk-assessment evaluation methods.** The FDA has strengthened requirements for manufacturers to generate data on the long-term impact of LAOs, with the aim of generating better evidence on the risks of opioid misuse, predictors of opioid addiction, and other issues. In addition, the FDA has sought to reassess the risk-benefit approval framework for opioid use.[185]

(d) **Increasing access to ADFs.** The OAP codified the FDA's goal to facilitate the development of abuse-resistant opioids and accelerate the approval process.[186]

(e) **Supporting access to better treatment.** Under the OAP, the FDA committed to support better access to treatment. For example, the FDA has reviewed options to increase access to overdose treatments, such as allowing over-the-counter availability of naloxone, and is endeavoring to support access to better pain management options, such as alternative (non-opioid) treatment options.[187] These efforts include the review of how "new, nonaddictive therapies that treat chronic pain or opioid addiction" can be designated as a breakthrough therapy (and therefore provided the potential for expedited market approval and access).[188]

83. The FDA's Risk Evaluation and Mitigation Strategies ("REMS") initiative is intended to ensure that prescribers are aware of the latest research regarding the risks and best practices associated with the prescribing of certain drugs, including opioids. The central element of an opioids REMS is "an education program for prescribers (e.g., physicians, nurse practitioners, physician

185 "FDA Opioids Action Plan," FDA, https://www fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm.

186 "FDA Opioids Action Plan," FDA, https://www fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm.

187 FDA Review Opioid Policies 2016.

188 "The Opioid Epidemic and the Food and Drug Administration: Legal Authorities and Recent Agency Action," Congressional Research Services, December 2018, p. 13; "Breakthrough Therapy," FDA, https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy. See also H.R. 6 §3001 (a-b).

assistants) and patients."[189] The FDA has published a "Blueprint" which outlines key messages and content to be conveyed to prescribers through the education program.[190] Using the Blueprint, education providers can "develop accredited [continuing education] in the manner they choose."[191] Core elements include a "Medication Guide"; the provision of "REMS-compliant training" and other "Elements to Assure Safe Use," which outline the medical actions and safety pre-requisites for a prescriber dispensing a drug; an "Opioid Analgesics REMS Patient Counseling Guide"; and a "Timetable for Submission of Assessments" to monitor the effectiveness of the REMS.[192] REMS thus help balance the "risk/benefit profile of certain opioid medications by requiring manufacturers to provide training and education to physicians regarding universal precautions in opioid prescribing, updated medication guides for each product, and patient counseling documents."[193] The FDA may require a REMS prior to the marketing authorization of a new product; it may also require a REMS for an existing approved product with updated safety information.[194]

84. In June 2018, the FDA sent safety labeling change notification letters to manufacturers of opioid products intended for use in an outpatient setting.[195] The letters required that manufacturers include new safety information regarding the REMS in the Boxed Warning and Warnings and Precautions sections of

189 76 FR 68766 (November 7, 2011).

190 "FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain," FDA, September 2018.

191 76 FR 68767 (November 7, 2011).

192 "Extended-Release (ER) And Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS)," FDA, https://www.fda.gov/media/83883/download, pp. 2-7.

193 See, for example, Barth et al. 2017, p. 12; Throckmorton, Douglas C., "FDA Policies and Actions Related to the Development and Use of Opioids to Treat Pain," FDA, 2016, p. 12. Note that REMS are an obligation of manufacturers; there is no opportunity for the participation of distributors.

194 "Risk Evaluation and Mitigation Strategies (REMS): Framework for Effective Patient Counseling on Medication Risks and Benefits," The Brookings Institution, August 2015, p. 2.

195 "New Safety Measures Announced for Immediate Release (IR) Opioids," FDA, https://www fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm491437.htm.

prescribing information, thus aiming to improve the "general lack of awareness" of the REMS among opioid prescribers.[196]

(b) DEA

85. The DEA administers and enforces Title II of the Comprehensive Drug Abuse Prevention and Control Act, and Title III of the Controlled Substances Import and Export Act (collectively the "CSA," legislated in 1970).[197] The CSA requires any "person who manufactures, distributes, dispenses, imports, or exports any controlled substance or who proposes to engage in the manufacture, distribution, dispensing, importation or exportation of any controlled substance" to register with the DEA, unless exempt.[198]

86. The CSA categorizes each controlled substance into one of five schedules based upon its potential for abuse, currently accepted medical use, and the degree of dependence the substance may cause.[199] Each schedule is subject to distinct regulatory controls. The DEA may transfer a drug between schedules if requested, following the evaluation of scientific and medical information and the recommendation of the Assistant Secretary for Health.[200] As shown on Exhibit III-1, the most widely prescribed opioids are schedule II. Schedule I opioids include heroin and certain compounds of fentanyl.[201]

---

196 "FDA announces enhanced warnings for immediate-release opioid pain medications related to risks of misuse, abuse, addiction, overdose and death," FDA News Release, March 22, 2016; "New Safety Measures Announced for Immediate Release (IR) Opioids," FDA, https://www fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm491437.htm.

197 77 FR 15234 (March 15, 2012).

198 21 U.S.C § 1301.11(a) (2009). Exempt parties include employees of the DEA, Customs Service, FDA, and other federal, state, or political subdivisions who are authorized to handle controlled substances as part of their official duties of employment (21 C.F.R. §§ 1301.24(a)(2), (b); 21 C.F.R. §§ 1301.22-1301.23). In addition, an individual who has legally obtained a controlled substance for their own use is exempt from DEA registration (21 U.S.C. § 822(c)).

199 "Controlled Substance Schedules: Definition of Controlled Substance Schedules," DEA, https://www.deadiversion.usdoj.gov/schedules/#define.

200 21 U.S.C § 811(a) (2018); 79 FR 49672 (August 22, 2014).

201 "Controlled Substances," DEA, May 2, 2019, https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf.

87. As mandated by the CSA, the DEA operates a quota system for products listed in schedules I and II.[202] Each controlled substance is assigned an aggregate production quota ("APQ"). The APQ designates the upper limit of national production of the controlled substance. It is established based on the DEA's assessment of the national need for a specific substance, taking into account data such as individual manufacturer requirements, net inventory and disposal trends, projected demand based on prescription audit data, and other factors affecting the "medical, scientific, research, and industrial" demand for the product.[203] Any interested parties, such as medical professionals, may submit written comments or objections to the DEA's determined APQs, and the DEA may (but is not required to) hold a public hearing to review the issues raised.[204]

88. APQs from 2006 forward for oxycodone and hydrocodone, the most widely prescribed opioids, are shown in Exhibits III-6 and III-7, respectively, apportioned to Ohio on the basis of population relative to the U.S. population. These are compared to actual deliveries to retail-facing customers in Ohio based on data provided by the DEA through its Automation of Reports and Consolidated Orders System ("ARCOS"). The apportioned APQ exceeds deliveries by a significant amount for both oxycodone and hydrocodone.

89. The DEA has a number of methods to address alleged violations of the CSA.

(a) **Letter of Admonition and Informal Hearings.** The DEA can issue a warning "Letter of Admonition" to any registrant suspected of violating the CSA. For example, in August 2009, the DEA issued Letters of Admonition to various prescribers, reiterating prescriber responsibilities under the CSA. These Letters emphasized the prescribers' "responsibility

---

202 The CSA requires the Attorney General to establish quotas for controlled substances (21 U.S.C. § 826 (2011)). The Attorney General delegated this authority to the DEA (21 C.F.R. § 1300.01(b) (2018)).

203 83 FR 32784 (July 16, 2014); Dang, Minh T., "Quotas," DEA, 2013, https://www.deadiversion.usdoj.gov/mtgs/man_imp_exp/conf_2013/dang_1.pdf ("Dang 2013"), p. 25; 21 CFR 1303.11 (a) (2018).

204 21 CFR 1303.11 (c) (2018).

for […] proper prescribing of controlled substances."[205] In addition, the DEA can hold an "Informal Hearing" with a registrant. Both Letters of Admonition and Informal Hearings allow the registrant an "opportunity to recognize and acknowledge their infractions, and immediately correct them."[206] Between fiscal years 2009 and 2013, the number of Letters of Admonition sent by the DEA to registrants increased from 394 to 1,296.[207]

(b) **Proceedings to deny, revoke or suspend registrations.** For certain violations of the CSA, the DEA has the authority to deny, revoke, or suspend licenses to handle controlled substances.[208] Before such action is taken, the DEA is required to provide the registrant with notice and an opportunity to demonstrate why the registration should not be "denied, revoked, or suspended," also known as an Order to Show Cause ("OTSC").[209] An OTSC can be issued if the DEA can show: (1) "an immediate threat that death, serious bodily harm, or abuse of a controlled substance will occur" due to the failure of the registrant to comply with the CSA's requirements, or (2) the "substantial likelihood" that such a threat will occur without an immediate suspension of a registration.[210] The OTSC provides the registrant an opportunity to submit a Corrective Action Plan ("CAP") to the DEA and appear at a formal hearing before a DEA Administrative Law Judge. If the DEA Administrative Law Judge decides to suspend or revoke a license, all controlled substances owned or possessed by the registrant may "be placed under seal […] until the time for taking an appeal has elapsed or until all appeals have been concluded

---

205 Letter from Joseph T. Rannazzisi, Deputy Assistant Administrator, Office of Diversion Control, to Practitioners, August 6, 2009, p. 2.

206 "Legal Authorities Under the Controlled Substances Act to Combat the Opioid Crisis," Congressional Research Service, December 18, 2018, ("CRS Report, 2018"), p. 20.

207 "More DEA Information about Registrants' Controlled Substances Roles Could Improve Their Understanding and Help Ensure Access," GAO, June 2015, https://www.gao.gov/assets/680/671562.pdf, ("GAO Report, 2015"), Table 34.

208 21 C.F.R. 1301.37 (c).

209 21 U.S.C. 824 (c).

210 CRS Report, 2018, p. 23.

[…]."[211] A revocation is finalized when all opportunities for judicial appeals have been exhausted; then all controlled substances owned by the registrant "shall be forfeited to the United States."[212] Between fiscal years 2009 and 2013, the number of OTSCs sent by the DEA declined from 74 to 45.[213]

(c) **Immediate suspension orders.** The DEA has the authority to suspend immediately any existing registration for a period of time, bypassing the requirement to provide the registrant with notice or opportunity to attend a formal hearing.[214] The suspension is effective until the conclusion of any judicial reviews.[215] Between fiscal years 2009 and 2013, the number of Immediate Suspension orders enforced by the DEA declined from 28 to 16.[216]

(d) **Criminal charges and financial penalties.** The CSA sets out several criminal provisions and financial penalties that apply to DEA registrants.[217] Between fiscal years 2009 and 2013, the number of drug diversion-related criminal investigations linked to the DEA declined from 813 to 634.[218] During the same time period, the total number of civil fines requested from pharmacies for violations of the CSA declined from 47 to 31, although the total dollar value of fines almost doubled from $7.0 million to $13.2 million.[219] Over the same time period, the total number of civil fines requested from distributors for violations of the CSA ranged

211 21 U.S.C. 824 (f).
212 21 U.S.C. 824 (f).
213 GAO Report, 2015, Table 37.
214 CRS Report, 2018, p. 23; 21 U.S.C. 824(d).
215 21 U.S.C. 824(d).
216 GAO Report, 2015, Table 37.
217 CRS Report, 2018, pp. 17, 23; 21 U.S.C. § 843(a).
218 GAO Report, 2015, Table 33.
219 GAO Report, 2015, Table 38.

from two to three per year, although the total dollar value of fines increased from $4.2 million to $80.0 million.[220]

90. In Ohio, the DEA has invoked its authority to suspend and/or penalize physicians and pharmacies in circumstances involving the alleged diversion of prescription opioids, as exemplified below.

(a) In 2015, the license of Dr. Syed Jawed Akhtar-Zaidi of Cuyahoga County was revoked by the DEA, due to evidence that continued "registration would be inconsistent with the public interest."[221] Specifically, the decision to rescind Dr. Akhtar-Zaidi's license was based on evidence that he had failed to maintain "accurate medical records" and had prescribed controlled substances without a "legitimate medical purpose."[222]

(b) In 2009, East Main Street Pharmacy ("Pharmacy") in Columbus, Ohio, was served with an Immediate Suspension Order ("ISO") by the DEA, following an OTSC earlier in the year. The ISO suspended the registration of the Pharmacy, alleging that its operations posed "an imminent danger to the public health and safety."[223] The ISO alleged that the sole pharmacist consistently filled out prescriptions for controlled substances "under circumstances indicating that the prescriptions were issued outside the usual course of professional practice."[224] For example, the DEA alleged that the pharmacist dispensed controlled substances for patients "travelling substantial distances to obtain the drugs" which should have indicated that these "controlled substances were likely to be diverted or used for other than legitimate medical purposes."[225]

---

220 GAO Report, 2015, Table 38.
221 80 FR 42996 (July 20, 2015).
222 80 FR 42962; 42964 (July 20, 2015).
223 72 FR 66150 (October 27, 2010).
224 72 FR 66149 (October 27, 2010).
225 72 FR 66150 (October 27, 2010).

F. Oversight of Opioids: State

(a) Boards of Pharmacy / Departments of Public Health

91. I understand that state Boards of Pharmacy ("BOPs") are the states' "primary regulator of pharmacies" and govern the conduct of pharmacists, pharmacy technicians, and overall pharmacy practice.[226] Although states have the primary authority to regulate pharmacy practice, pharmacies are also regulated by federal laws, such as the CSA.[227]

92. The Ohio BOP is the sole agency in Ohio "responsible for administering and enforcing laws governing the practice of pharmacy and the legal distribution of drugs."[228] The Ohio BOP is mandated by federal regulations and the Ohio Revised Code to "investigat[e] and present evidence of violations of any of the federal or state drug laws" for the "prosecution of the offender."[229] As such, in addition to pharmacists and pharmacy technicians, the Ohio BOP also governs the license of manufacturers, distributors, and wholesalers of controlled substances.[230]

93. The Ohio BOP has the power to revoke the licenses of pharmacists found to be illegally distributing or dispensing controlled substances. For example, between 2011 and 2014, the Ohio BOP revoked the licenses of 15 pharmacists due to violations involving improper dispensing of prescription drugs.[231] It is not apparent how many of these revocations were related to prescription opioids.

---

226 "State regulation of compounding pharmacies," National Conference of State Legislatures, http://www ncsl.org/research/health/regulating-compounding-pharmacies.aspx.

227 Darvey, Diane L., "Legal Handbook for Pharmacy Technicians," *American Society of Health-System Pharmacists*, 2008, p. 4.

228 "Welcome to the State of Ohio Board of Pharmacy," Ohio BOP, https://pharmacy.ohio.gov/.

229 "Law Enforcement," Ohio BOP, https://pharmacy.ohio.gov/LawEnforcement/General.aspx.

230 Schierholt, Steven W., "Pain Management Clinics in Ohio: A special report (July 2011-December 2014)," Ohio State Board of Pharmacy, July 2011, p. 2.

231 Penin, Jonathan et al., "Strategies and policies to address the opioid epidemic: A case study of Ohio," *Journal of American Pharmacists Association*, 57:2, 2017 ("Penin 2017"), p. S149; "Ohio state, local officials working to prevent 'pill mills'," Ohio Task Force Commanders Association, https://otfca net/ohio-state-local-officials-working-to-prevent-pill-mills/. See also Expert Report of Dennis Wichern, May 10, 2019 ("Wichern Report"), Section III.G.

(b) Medical Boards

94. I understand that the licensure and practice of medicine by physicians are governed by SMBs.[232] The right to practice medicine is granted by individual states through state laws and regulations, as established by a State Medical Practice Act.[233] In general, this Act defines "unprofessional, improper, incompetent, unlawful, fraudulent and/or deceptive practice of medicine" such that the health and welfare of the public are put at risk.[234] SMBs are authorized to evaluate and penalize physicians if their practice of medicine violates the terms of the Act and can consequently enforce suspension or revocation of physicians' licenses to practice.[235] A significant number of SMB actions involve "misuse and mis-prescribing of controlled substances," including opioids.[236]

95. Under the mandate of the Medical Practices Act and the Ohio Revised Code, the State Medical Board of Ohio ("Ohio SMB") licenses and governs the practice of physicians and therapists in Ohio. The Ohio SMB is authorized to "investigat[e] complaints against applicants and licensees and tak[e] disciplinary action against those who violate the public health and safety standards."[237] For example, according to the Ohio Administrative Code, "prescriptions that exceed the five or

---

232 Carlson, Drew and James N. Thompson, "The Role of State Medical Boards," *Ethics Journal of the American Medical Association*, 7:4, 2005, ("Carlson and Thompson 2005"), p. 2.

233 Carlson and Thompson 2005, p. 2.

234 "Essentials of a State Medical and Osteopathic Practice Act," Federation of State Medical Boards, 2015, p. 3. Derek Siegle, Executive Director of the Ohio High Intensity Drug Trafficking Area Program, testified that "the medical board, the pharmacy board, the diversion units" can stop "pill mills" from operating (Deposition of Derek Siegle, January 23, 2019, pp. 127-128). He also stated that "law enforcement," not private companies, has the ability to arrest diverters, and that "the state medical board" has the ability to revoke the licenses of doctors engaged in diversion (Siegle Deposition, pp. 130-131).

235 Carlson and Thompson 2005, pp. 3-4.

236 Dineen, Kelly, K. and James M. DuBois, "Between a Rock and a Hard Place: Can Physicians Prescribe Opioids to Treat Pain Adequately While Avoiding Legal Sanction?," *American Journal of Law and Medicine*, 42:1, 2016, p. 9.

237 "Agency Mission and Goals," Ohio SMB, https://med.ohio.gov/The-Board/Agency-Mission-and-Goals.

seven day supply or thirty [MME] average daily dose are subject to additional review by the state medical board."[238]

96. Between 2011 and 2018, the Ohio SMB took disciplinary action against more than 300 practitioners for "violations involving improper prescribing of prescription drugs."[239] From 2011 to 2014, the SMB revoked the licenses of 61 physicians for violations specifically involving improper prescribing of prescription drugs; 51 of these were permanent revocations.[240] For example, the Ohio SMB suspended and later permanently revoked the medical license of Dr. Juan Michael Hernandez of Cuyahoga County for failure to "conform to minimal standards of care."[241] Dr. Hernandez was disciplined for violations related to the Ohio SMB's prescribing standards on controlled substances, such as a failure to "employ acceptable scientific methods in the selection of drugs, as well as the failure to comply with the standards and procedures of operating a pain management clinic."[242]

(c) Prescription Drug Monitoring Programs

97. PDMPs are state-level programs, often administered by BOPs or Departments of Public Health, designed to prevent or reduce instances of diversion of controlled substances and other potentially abused products, including opioids. PDMPs serve two functions: (i) provide the state agency with information that may identify unusual prescribing and dispensing behavior; and (ii) allow health care providers access to information on previous prescriptions issued to patients in order to ensure that patients are not misusing the drugs.[243] PDMPs are designed

238 Ohio Admin. Code § 4731-11-13 (August 31, 2017).

239 "Combating the Opiate Crisis in Ohio 2011-2018," Ohio Governor's Cabinet Opiate Action Team, September 2018, p. 2. See also Wichern Report, Section III.G.

240 Penin 2017, p. S149; "Ohio state, local officials working to prevent 'pill mills'," Ohio Task Force Commanders Association, https://otfca net/ohio-state-local-officials-working-to-prevent-pill-mills/.

241 MCKPUB00028872-873 at 872.

242 MCKPUB00028872-873 at 873.

243 "What States Need to Know about PDMP about PDMPs," CDC, https://www.cdc.gov/drugoverdose/pdmp/states html; "State Profiles," Prescription Drug Monitoring Program Training and Technical Assistance Center, https://www.pdmpassist.org/content/state-profiles.

to be accessed by physicians and pharmacists in order to assess whether a prescription for a controlled substance may be intended for non-medical purposes.[244] For example, a physician may verify that a patient has not recently received a prescription from another physician; a pharmacist may check that a patient has not filled the same prescription at other pharmacies. As of January 2019, PDMPs were administered by every state, with the exception of Missouri.[245]

98. Run by the Ohio BOP, OARRS was established in 2006 "[t]o address the growing misuse and diversion of prescription drugs."[246] OARRS collects information on "outpatient prescriptions for controlled substances … dispensed by Ohio-licensed pharmacies."[247] This information is collected directly from dispensers who are currently required to report transactions every 24 hours.[248] OARRS data include the name of the patient, name of the prescriber, the name of the drug being dispensed, the quantity of the drug, and the number of days supplied.[249] Since April 2015, data from OARRS must be accessed by prescribers "[b]efore initially prescribing or personally furnishing an opioid analgesic" and at intervals less than 90 days for patients undergoing a course of opioid treatment exceeding 90 days.[250] In 2011, there were approximately 1.8 million queries for patient

---

244 "Prescription Drug Monitoring Programs: Critical Decision Support Tools to Respond to the Opioid Crisis," National Alliance for Model State Drug Laws, https://namsdl.org/wp-content/uploads/Congressional-Briefing-Final-Agenda-and-Presentation.pdf, p. 8.

245 St. Louis County does have its own PDMP ("Prescription Drug Monitoring Programs: Critical Decision Support Tools to Respond to the Opioid Crisis," National Alliance for Model State Drug Laws, https://namsdl.org/wp-content/uploads/Congressional-Briefing-Final-Agenda-and-Presentation.pdf, p. 6).

246 "What is OARRS?," OARRS, https://www.ohiopmp.gov/About.aspx.

247 "What is OARRS?," OARRS, https://www.ohiopmp.gov/About.aspx.

248 "Ohio Data Submission Dispenser Guide," Ohio BOP, October 2017, ("Ohio Data Submission Dispenser Guide 2017"), p. 5, https://www.ohiopmp.gov/Documents/Reporting%20to%20OARRS.pdf. Apparently, transaction reporting was required to be at least twice monthly until 2011, then at least weekly until 2017 (Deposition of Chad Garner, Director of OARRS Program, Ohio BOP, November 14, 2018 ("Garner Deposition"), p. 141).

249 Ohio Data Submission Dispenser Guide 2017, pp. 22-36.

250 "Mandatory OARRS Registration and Requests," Ohio BOP, https://www.pharmacy.ohio.gov/Documents/Pubs/Special/OARRS/Mandatory%20OARRS%20Registration%20and%20Requests.pdf.

information from OARRS; by 2017, these queries had increased by more than 40 times, to 89 million.[251]

99. The Ohio BOP monitors compliance with OARRS reporting requirements by matching the list of pharmacies submitting data to OARRS against its own list of pharmacies, typically running these reports weekly and contacting pharmacies that have failed to submit a report. OARRS also uses thresholds to measure whether a pharmacy submits all the required data and will reject a record that is missing data or below the threshold of information needed. These pharmacies will receive a letter that identifies the records rejected; the records must be corrected and resubmitted.[252]

(d) Pain Management Clinic Laws

100. I understand that starting in the mid-to-late 2000s, some state governments introduced legislation to regulate pain management clinics. By 2013, nine states had Pain Management Clinic Laws ("PMCLs") in effect;[253] in June 2018, the number had increased to 12.[254] According to one source: "Although there is substantial heterogeneity across states, regulations associated with PMCLs typically provide for requirements concerning the ownership, the licensing procedures, the operational standards and the personnel qualification of pain management clinics, facilities or practice locations."[255]

---

251 "2017 Annual Report Executive Summary," OARRS, https://www.ohiopmp.gov/documents/Annual%20Report%20(2017)%20-%20Executive%20Summary.pdf.

252 "Frequently Asked Questions," OARRS, https://www.ohiopmp.gov/FAQ.aspx; Garner Deposition, pp. 141-143.

253 These states are Florida, Georgia, Kentucky, Louisiana, Mississippi, Ohio, Tennessee, Texas, and West Virginia (National Alliance for Model State Drug Laws, "Prescription Drug Abuse, Addiction and Diversion: Overview of State Legislative and Policy Initiatives," April 2014, https://web.archive.org/web/20161020173410/http://www namsdl.org/NAMSDL%20Part%202%20Revised%20April%204%202014.pdf, p.10).

254 The additional states included Arizona, Alabama, and Wisconsin ("Pain Management Clinic Laws," Prescription Drug Policy and Abuse System, http://pdaps.org/datasets/pain-management-clinic-laws).

255 Deiana, Claudio and Ludovica Giua, "The US Opidemic: Prescription Opioids, Labour Market Conditions and Crime," MPRA Research Paper, March 2018, ("Deiana and Giua 2018"), p. 8.

101. In Ohio, legislation was introduced to regulate pain management clinics.[256] In 2011, Ohio House Bill 93 (the "2011 Bill") was passed which defined pain management clinics as facilities where "the primary component of practice is treatment of pain or chronic pain; [and] the majority of patients of the prescribers at the facility are provided treatment for pain or chronic pain."[257] The 2011 Bill required each pain clinic to: (i) register with the BOP as a "Terminal Distributor of Dangerous Drugs;" (ii) have an ownership group consisting of "one or more physicians;" (iii) run criminal background checks on all prospective owners and employees; (iv) limit all prescriptions for a controlled substance to a 72-hour supply; and (v) report all transactions to the OARRS program.[258]

102. The 2011 Bill empowers the Ohio BOP to "impose a fine of not more than five thousand dollars on a person" who fails to comply with the operational requirements of a pain management clinic.[259] Any non-compliant physicians may also be subject to other SMB disciplinary actions, such as "suspension, without a prior hearing, of the physician's authority to practice medicine."[260] Similarly, the Ohio BOP can suspend the license of a non-compliant terminal distributor without a prior hearing, although if the "license holder is a physician, the act requires the Pharmacy Board to first consult with the secretary of the Medical Board or, if the secretary is unavailable, another physician member of the Medical Board."[261]

103. An amendment to the 2011 Bill, passed in 2017, established operational standards for physicians to meet, including that physicians maintain a daily log of patients

---

256 "Ohio passes law cracking down on pill mills," MD Magazine, June 01, 2011, https://www mdmag.com/medical-news/ohio-passes-law-cracking-down-on-pill-mills; Rutkow, Lainie et al., "More States Should Regulate Pain Management Clinics to Promote Public Health," *American Journal of Public Health*, 107:2, 2017, p. 240.

257 "Am. Sub. H.B. 93 Act Summary," Ohio Legislative Service Commission, May, 2011, 054https://www.lsc.ohio.gov/documents/gaDocuments/analyses129/11-hb93-129.pdf, ("Am Sub. H.B. 93 Act Summary"), p. 9.

258 Ohio State Board of Pharmacy Newsletter, May 2011, https://www.pharmacy.ohio.gov/Documents/Pubs/Newsletter/2011/State%20Board%20Newsletter%20(May%202011).pdf.

259 Ohio Admin. Code § 4729-552(D) (August 29, 2017).

260 Am Sub. H.B. 93 Act Summary, p. 9.

261 Ohio Admin. Code § 4729-571 (August 29, 2019).

visiting the clinic and patient records contain "sufficient information to identify the patient, support the diagnosis, justify the treatment and document … the results."[262] The 2017 amendment also introduced rules that established that clinics should be owned by physicians who are certified pain specialists and should undertake training every two years, including courses related to potential for addiction.[263]

G. Other Regulatory Obligations on Supply Chain Participants

(a) Storage and Handling Requirements

104. I understand that minimum security standards for the storage and handling of opioids and other controlled substances by pharmacists and other registered persons (e.g., practitioners) are set out by the DEA. The DEA requires that controlled substances be "adequately safeguarded" and that "controlled substances must be stored in a securely locked cabinet of substantial construction."[264] To reduce the opportunity for theft and diversion of controlled substances, pharmacists should endeavor to establish additional procedures to reduce unauthorized individuals' access and to implement an effective alarm system.[265]

105. In addition to regulations on the storage and handling of controlled substances, there also exist regulations on how controlled substances must be disposed. The Secure and Responsible Drug Disposal Act states that "authorized manufacturers, distributors, reverse distributors, [and] narcotic treatment programs (NTPs)" can dispose of a controlled substance though "mail-back programs" or "collection receptacles."[266] End users can also carry their "unwanted pharmaceutical controlled substances to an authorized retail pharmacy or other authorized

---

262 Ohio Admin. Code. § 4731.29.01(E)(1); Ohio Admin. Code. § 4731.29.01(E)(6)(a).

263 Ohio Admin. Code. § 4731.29.01(B).

264 "Controlled Substances Security Manual," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/sec/sec_req.htm.

265 "Controlled Substances Security Manual," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/sec/sec_req.htm.

266 79 FR 53520 (September 9, 2014).

collector location … for disposal."[267] With regards to the actual destruction, controlled substances must be rendered "non-retrievable" (such that they are "unusable").[268]

(b) Suspicious Order Monitoring

106. I understand that the DEA regulations require distributors and manufacturers that are registered with the DEA to design and operate systems to identify suspicious orders of controlled substances and to notify their local DEA Field Division about suspicious orders upon discovery ("Reporting Requirement").[269] Distributors are required to design and operate a system that flags suspicious orders including "orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency."[270] The regulations, however, provide no specific guidance on the definitions of "unusual size," "normal pattern," or "unusual frequency."

107. In 2005, the DEA established an Internet Distributor Initiative Program to "increase the awareness of DEA registrants regarding their obligations and possible role in the illegal distribution of pharmaceuticals via the Internet."[271] This program entailed individual meetings between the DEA and several distributors (including McKesson, Cardinal, and ABDC), reviewing each distributor's reporting responsibilities under the CSA.[272] Participants received a package of materials which included a PowerPoint presentation titled "Internet

---

267 79 FR 53521 (September 9, 2014).

268 79 FR 53548 (September 9, 2014).

269 See 21 CFR 1301.74 (b). Prior to 2005, registrants (in this case, distributors) were obligated to identify suspicious orders as those that diverged from customer and circumstance norms, e.g., "a [new] customer who is vague about its firm's address, telephone number and reason for desiring a listed chemical" (CAH_MDL_PRIORPR0D_H0USE_0002207-298 at 250). In October 2008, the Ryan Haight Online Pharmacy Consumer Protection Act was introduced and amended the CSA by including new "provisions to prevent the illegal distribution and dispensing of controlled substances by means of the Internet." (74 FR 15596 (April 6, 2009)).

270 21 CFR 1301.74 (b). At times there may have been requirements to block, or not ship, certain orders that are found to be in aid of diversion ("Distributor Initiative: A National Perspective," Office of Diversion Control, October 22, 2013, p. 23).

271 US-DEA-00002454-461 at 459-460.

272 "Red Flags and Warning Signs Ignored: Opioid Distribution and Enforcement Concerns in West Virginia," Energy and Commerce Committee, December 19, 2018, p. 6.

Pharmacy Data", two agency final orders revoking the registrations of internet pharmacies; guidance documents from the DEA, the American Medical Association, and the Federation of State Medical Boards regarding the dispensing and purchasing of controlled substances over the internet; and copies of relevant statutes, 21 U.S.C. § 823 and 21 C.F.R. § 1301.74(b).[273]

108. Subsequent to these meetings, the DEA sent two letters to DEA-registered distributors and manufacturers relating to their obligations under the aforementioned statutes.[274] The first such letter, dated September 27, 2006 ("2006 DEA Letter"), provided examples of the "Circumstances That Might be Indicative of Diversion."[275] These circumstances included a pharmacy: (i) "Ordering excessive quantities of a limited variety of controlled substances;" (ii) "Ordering a limited variety of controlled substances in quantities disproportionate to the quantity of non-controlled medications ordered;" (iii) "Ordering excessive quantities of a limited variety of controlled substances in combination with excessive quantities of lifestyle drugs;" and (iv) "Ordering the same controlled substance from multiple distributors."[276]

109. A second letter, dated December 27, 2007 ("2007 DEA Letter") stated: "Registrants that rely on rigid formulas to define whether an order is suspicious may be failing to detect suspicious orders."[277] Additional orders that should be flagged include "unusually large orders from the beginning" of the relationship between a buyer and a distributor; orders that "were solely for one highly abused controlled substance" relative to other substances; and orders that deviate from

---

273 72 FR 36487, 36492 (July 3, 2007); MCKMDL00496859-875 at 859; US-DEA-00000352-366 at 352-353; US-DEA-00003880.

274 A 2006 DEA letter was sent to every DEA-registered distributor (MCKMDL00478906-909 at 906); a 2007 DEA letter was sent to every DEA-registered distributor and manufacturer (MCKMDL00478910-911 at 910).

275 MCKMDL00478906-909 at 906, 908.

276 MCKMDL00478906-909 at 908.

277 MCKMDL00478910-911 at 911.

"the registrant's customer base and the patterns throughout the relevant segment of the regulated industry."[278]

110. Both the 2006 DEA Letter and the 2007 DEA Letter state that registrants have a responsibility to investigate a suspicious order and resolve their suspicions prior to completing the sale. The 2006 DEA Letter lists questions that "[a] distributor seeking to determine whether a suspicious order is indicative of diversion of controlled substances to other than legitimate medical channels may wish to inquire [of] the ordering pharmacy".[279] The 2007 DEA Letter states that "[r]egistrants must conduct an independent analysis of suspicious orders prior to completing a sale to determine whether the controlled substances are likely to be diverted from legitimate channels."[280] The 2007 DEA letter also states that distributors must report suspicious orders "when discovered by the registrant".[281]

278 MCKMDL00478910-911.

279 MCKMDL00478906-909 at 908. These ten inquiries are listed below.
1. What percentage of the pharmacy's business does dispensing controlled substances constitute?
2. Is the pharmacy complying with the laws of every state in which it is dispensing controlled substances?
3. Is the pharmacy soliciting buyers of controlled substances via the Internet or is the pharmacy associated with an Internet site that solicits orders for controlled substances?
4. Does the pharmacy, or Internet site affiliated with the pharmacy, offer to facilitate the acquisition of a prescription for a controlled substance from a practitioner with whom the buyer has no pre-existing relationship?
5. Does the pharmacy fill prescriptions issued by practitioners based solely on an on-line questionnaire without a medical examination or bona-fide doctor-patient relationship?
6. Are the prescribing practitioners licensed to practice medicine in the jurisdictions to which the controlled substances are being shipped, if such a license is required by state law?
7. Are one or more practitioners writing a disproportionate share of the prescriptions for controlled substances being filled by the pharmacy?
8. Does the pharmacy offer to sell controlled substances without a prescription?
9. Does the pharmacy charge reasonable prices for controlled substances?
10. Does the pharmacy accept insurance payment for purchases of controlled substances made via the Internet?

280 MCKMDL00478910-911 at 910.

281 MCKMDL00478910-911 at 910 (emphasis in original).

IV. OVERVIEW OF PHARMACEUTICAL DISTRIBUTION

111. The prescription opioids at issue in this litigation are principally dispensed by retail pharmacies and taken by patients themselves. This section summarizes the flow of prescription opioid drugs from manufacturer to patient; the corresponding flow of payments; and the flow of information relating to the distribution of the products. A relevant distinction with respect to the flow of product and payments is between single-source and multiple-source drugs. Single-source, or "branded," drugs are sold under a brand name, are typically available from only one company, and are generally patent-protected. Multi-source drugs are those for which generic equivalents are available, because these are not patent-protected and are available from multiple companies.

A. Flow of Products

112. The flow of products associated with an opioids prescription is shown in Exhibit IV-1. It is the prescription that pulls product through the pharmaceutical distribution channel. Patients see their physician and, following an examination, may be prescribed an opioid for pain. Physicians can provide prescriptions on paper directly to the patient, electronically, or by phoning a pharmacy directly. Office-based physicians typically only prescribe opioids; they do not also dispense them.[282]

113. As discussed above, physicians must possess a DEA registration to prescribe controlled substances.[283] The DEA has the authority to suspend or revoke for any period of time a physician's DEA registration and thus remove the physician's

---

282 Certain office-based physicians also administer pharmaceutical treatments in the office setting. For example, certain physicians perform surgery in-office and may administer anesthesia. Physicians also may dispense and administer drugs such as methadone for the treatment of substance abuse in-office as part of a medication assisted treatment ("MAT") program for opioid use disorder. (See "Methadone," Substance Abuse and Mental Health Services Administration ("SAMHSA"), https://www.samhsa.gov/medication-assisted-treatment/treatment/methadone; "Medication and Counseling Treatment," SAMHSA, https://www.samhsa.gov/medication-assisted-treatment/treatment#otps.)

283 "Registration Applications," DEA, https://www.deadiversion.usdoj.gov/drugreg/faq htm#1.

ability to prescribe opioids.[284] For schedule II products, DEA requirements permit physicians to prescribe refills and process telephone orders in emergency situations only.[285] Prescriptions for schedule III through V products may be refilled up to five times in six months; these scripts may by written, communicated over the phone, or faxed.[286]

114. Retail and mail-order pharmacies dispense prescription drugs to patients presenting a prescription. Pharmacists provide information on drug risks, drug interactions, and proper use of products; they may also check the patient's medication record where appropriate.[287] In Ohio, pharmacists may substitute a generic equivalent for a branded drug; however, they cannot add or change a dosage form, strength, quantity, or directions for use without consultation and agreement of the prescribing practitioner.[288] I understand that pharmacies face heightened security requirements for the storage of controlled substance products. Pharmacies have the option of storing controlled substances in a securely locked cabinet of substantial construction, or concealing them by dispersal throughout their stock of non-controlled substances.[289]

115. Pharmacies generally acquire drugs from distributors, although some chain pharmacies have their own wholesaling function.[290] In 1999, it was estimated there were more than 10,000 prescription drugs and biologics available on the

---

284 21 CFR 1301.36(a).

285 Nonetheless, federal regulations permit the issuance of multiple prescriptions to a patient authorizing up to a total of a 90-day supply of a schedule II substance ("Practitioner's Manual – Section V," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section5.htm).

286 "Prescriptions," DEA, https://www.deadiversion.usdoj.gov/faq/prescriptions.htm.

287 "The Role of the Pharmacist in the Health Care System," WHO, http://apps.who.int/medicinedocs/en/d/Jh2995e/1.6.2 html; "What does a pharmacist do?" University of Iowa College of Pharmacy, https://pharmacy.uiowa.edu/what-does-pharmacist-do.

288 "For Pharmacists," Ohio BOP, https://www.pharmacy.ohio.gov/FAQ/Pharmacists.aspx.

289 "Security Requirements For Practitioners," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/sec/sec_req.htm.

290 Brooks, John M. et al., "Retail Pharmacy Market Structure and Performance," *Inquiry*, 45, 2008, p. 79; "CVS/pharmacy's Indiana Distribution Center Is First Facility in Retail Pharmacy Industry to Receive Verified Accreditation for Wholesale Distributors from the National Association of Boards of Pharmacy," CVS Health News Release, February 8, 2006.

market.[291] These include products in a wide range of therapeutic categories, a great number of which are shipped from manufacturers to pharmacies via distributors.

116. Certain self-warehousing pharmacies ceased distribution of certain opioids in 2014. For example, in 2014, Rite Aid ceased shipping hydrocodone combination products to its retail pharmacies and began to use McKesson as its distributor for these products, having already used McKesson for schedule II products prior to 2014.[292] Walmart ceased warehousing controlled substances in 2014 and began to use McKesson as its distributor.[293] Discount Drug Mart ceased warehousing controlled substances in 2014 and began to use Cardinal as its distributor.[294]

117. I understand that with respect to controlled substances, the DEA requires manufacturers and distributors to adhere to certain safety measures to avoid theft. In small quantities, schedule II products may be stored in a safe or steel cabinet provided it has security features including an alarm system, manipulation resistant locks, and it is secured to the ground. Otherwise, schedule II products must be stored in a vault with security features including a reinforced concrete perimeter, an advanced alarm system, self-closing and self-locking entrances, and locks resistant to manipulation.[295] Schedule III through V products may be stored in a safe, steel cabinet, or vault as described for schedule II products, or in a building with perimeter security, an alarm system, self-closing and self-locking doors, and locks controlled by a limited number of employees. Schedule III through V products also may be stored in a cage in a building with steel fabric walls, or in an enclosure, storage area, or building approved by the DEA Administrator.[296]

---

291 Institute of Medicine, *Preventing Medication Errors*, National Academies Press, 2007, p. 51.

292 Deposition of Debra Ann Chase, Control Cage Partner, Rite Aid's Perryman Distribution Center at Rite Aid, January 4, 2019, p. 68.

293 Deposition of Roxanne Reed, Senior Manager, Health and Wellness Compliance, Controlled Substances at Walmart, January 10, 2019, pp. 274, 277.

294 Deposition of Jill A. Strang, Pharmaceutical Buyer and Pharmacy Warehouse Supervisor, Discount Drug Mart, January 3, 2019, pp. 110-111.

295 21 CFR 1301.72(a)(1-3).

296 21 CFR 1301.72(b)(1-8).

118. The product dispensed by the pharmacy originates with a manufacturer. Manufacturers typically sell single-source drugs to distributors and more rarely directly to pharmacies. Generic drugs are more commonly sold directly to pharmacies, in addition to being sold through distributors.[297]

B. Flow of Payments

119. The flow of payments associated with filling an opioids prescription is depicted in Exhibit IV-2. Distributors tend to purchase branded and generic drugs from manufacturers at a list price, referred to as Wholesale Acquisition Cost ("WAC"), often less a two percent discount for prompt payment.[298] Distributors tend to sell single-source products to pharmacies with a minimal markup.[299] In the case of generic products and certain branded products, pharmacies may have agreements with manufacturers specifying price concessions based on certain criteria (e.g., volume discounts based on sales targets). The distributor then receives the pharmacy's negotiated price and "charges back" to the manufacturer the difference between this price and the distributor's cost, a transaction known as a "chargeback".

120. As discussed above, certain pharmacies may purchase generic products directly from the manufacturer. As pharmacies generally stock only one generic version of a drug, the generic manufacturers compete to be the version stocked and thus dispensed by the pharmacy. This competition tends to be played out on price, portfolio, and service dimensions, such as the timeliness and constancy of supply. The pharmacy also may continue to stock the original branded product for those instances when a generic version is not dispensed.

---

297 See, for example, "Follow the Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain," Kaiser Family Foundation, March 2006, p. 4; Fri, Perry, "Understanding the Pharmaceutical Supply Chain," Healthcare Distribution Management Association, July 22, 2015, slide 7; Fein, Adam, "Will Walgreens bypass Cardinal Health?," June 27, 2012, https://www.drugchannels.net/2012/06/will-walgreens-bypass-cardinal-health html.

298 Berndt, Ernst R. and Joseph P. Newhouse, "Pricing and Reimbursement in U.S. Pharmaceutical Markets," *Oxford Handbook of the Economics of the Biopharmaceutical Industry*, April 2012, ("Berndt and Newhouse 2012"), p. 218.

299 Berndt and Newhouse 2012, p. 218.

121. Pharmacies receive payment for pharmaceuticals from patients and third-party payors ("TPPs"). TPPs typically include health insurers, including Medicare and Medicaid, and pharmaceutical benefits managers ("PBMs"), who administer pharmaceutical benefits on behalf of health insurers and managed care organizations ("MCOs"). The amount of the pharmacy's reimbursement for a prescription dispensed to an insured patient is based on a contract between the TPP and the pharmacy. This contract defines how much the pharmacy is to collect from the patient as the out-of-pocket cost ("OOP")[300] and how much the pharmacy will be paid by the TPP. For patients who pay without insurance, the pharmacy sets the retail price of the product or the patient may pay using a coupon card or other such discount program, including, for example, GoodRx.[301] Some pharmacies also offer discount programs for generic products, which may or may not require a membership.[302]

122. As noted above, manufacturers are paid by the direct purchasers of their product, typically wholesalers and retailers. In addition, however, branded manufacturers also make certain rebate or reimbursement payments associated with the dispensing of their products. First, manufacturers may offer patients assistance with the OOP cost for the prescription; copay cards are an example.[303] Second, manufacturers may offer rebates to TPPs for formulary placement.

123. TPPs often use a prescription drug formulary which, in the case of PBMs, is set or approved by the health insurer or MCO.[304] The formulary is a list of drugs for which the TPP will reimburse under various conditions. The formulary defines

---

300 The OOP cost is typically a fixed dollar amount, known as a copayment, or it may be a percentage of the retail price for the product, known as coinsurance. Some insured patients may pay the full retail price of the pharmaceutical as part of the deductible related to their prescription drug benefit.

301 "Stop paying too much for your prescriptions," GoodRx, https://www.goodrx.com/.

302 See, for example, Walmart's $4 generics program ("Walmart Rx Program Guide to Low-Cost Prescriptions," Walmart Apollo, LLC, Effective November 28, 2018, https://i5.walmartimages.com/dfw/4ff9c6c9-e286/k2-_85e442c0-01c0-40e8-ae97-06162066b801.v1.pdf).

303 Choudhry, Niteesh K. et al., "Drug Company–Sponsored Patient Assistance Programs: A Viable Safety Net?," *Health Affairs*, 28:3, 2009, pp. 827, 829.

304 Robinson, James C., "Insurers' Strategies For Managing The Use And Cost of Biopharmaceuticals," *Health Affairs*, 25:5, 2006, p. 1205.

the OOP cost that an insured patient must pay and any conditions that must be satisfied in order for the prescription to be reimbursed. Formularies often have three or more tiers, with the OOP cost increasing at higher tier levels: Tier 1 products tend to be generics, Tier 2 products tend to be preferred brands, and Tier 3 products tend to be non-preferred brands. With the advent of higher-cost specialty drugs and the introduction of prescription drug benefits for Medicare patients under the Medicare Prescription Drug, Improvement, and Modernization Act in 2003, TPPs began to offer formularies with more tiers, up to Tier 6.[305] In addition to setting the OOP cost, the formulary might also set reimbursement criteria for a product. These criteria may include quantity limits, limits on days of supply dispensed at a time, prior approval requirements, requirements for step-therapy (in order for Product B to be reimbursed, it must be shown that a patient has tried Product A with undesirable results), or a requirement that the prescription be written by a specialist.[306]

124. Formularies tend to be set by Pharmacy and Therapeutics ("P&T") Committees. These committees are staffed by specialists in their medical disciplines. On a regular basis, they review each therapeutic category, such as narcotic analgesics (the therapeutic category including opioids) at Medical Mutual of Ohio.[307] The P&T Committee will consider new products launched since the last review, consider the results of clinical trials and other relevant data, and make recommendations regarding which products should be covered and under what criteria.

---

305 "H.R.1 - Medicare Prescription Drug, Improvement, and Modernization Act of 2003," Congress.gov, https://www.congress.gov/bill/108th-congress/house-bill/1.

306 "Formulary Management," Academy of Managed Care Pharmacy, http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9298.

307 "2019 Prescription Drug Formulary: Basic/Basic Plus," Medical Mutual, https://www medmutual.com/~/media/MedMutual/Files/IndividualsFamilies/2019/2019%20Basic%20Plus%20Formulary.ashx, p. 44.

C. Flow of Information

125. Throughout the pharmaceutical supply chain, each party holds certain information, which may not be visible to the other parties; this is especially the case with respect to prescription opioids. This flow of information is depicted on Exhibit IV-3.

(a) Information Available to Physicians, Pharmacies, Distributors, Manufacturers, and TPPs

126. Beginning with the physician, I note that the physician's role in the distribution of opioids is to evaluate a patient and prescribe medications as appropriate, taking into account a patient's medical and pharmacological history. Physicians and other health care providers ("HCPs") have face-to-face interactions with their patients with whom they examine and question, and often have long-term trusted relationships with. They exercise their informed and experienced medical judgment, based on the circumstances of each individual patient, in deciding the appropriate therapy, including what drugs to prescribe, in what dosages, in what quantity, and over what period of time.[308] In some cases, this may involve prescribing drugs "off label" to treat conditions other than the indications for which the drug was approved by the FDA. Nonetheless, physicians do not know whether a prescribed drug is actually used as prescribed by the patient, whether the drug is used more or less than as prescribed, or whether the drug is given or sold to others for non-medical use; such behavior, however, might become evident to the physician in future visits with the patient.[309]

127. Specifically with respect to opioids, HCPs in many states also received access over time to PDMPs;[310] in Ohio, HCPs specifically received access to OARRS.

---

308 Pollock, Madelyn et al., "Appropriate Prescribing of Medications: An Eight-Step Approach," *American Family Physician*, 75, 2007, p. 231; Deposition of Joan M. Papp, M.D., Medical Director of the Office of Opioid Safety, MetroHealth, February 5, 2019 ("Papp Deposition"), pp. 63-64.

309 Papp Deposition, p. 56.

310 Vestal, Christine, "States require doctors to use prescription drug monitoring systems for patients," *Washington Post*, January 15, 2018 ("Vestal 2018"), https://www.washingtonpost.com/

In Ohio, HCPs were required to input each prescription of a controlled substance since the inception of its PDMP in 2006.[311] Further, since April 2015, HCPs also were required to request patient information covering the last twelve months from OARRS before initially prescribing a controlled substance and at intervals less than 90 days for patients undergoing a course of opioid treatment exceeding 90 days.[312]

128. The Ohio SMB uses audit reports provided by the State of Ohio Board of Pharmacy to monitor HCP compliance with OARRS requirements. These reports include identifying HCPs who wrote an opioid prescription for more than a seven-day supply and who had no OARRS query recorded for a 90-day period preceding the issuance of that prescription. Periodically, identified HCPs are sent a warning letter and possible action against their licenses and/or a monetary fine can occur.[313]

129. In general, PDMPs require the reporting of opioid prescriptions within one business day of being dispensed.[314] The information required includes the identity of the patient (name, address, birthdate, gender, driver's license number), the prescribing physician (including DEA number), the dispensing pharmacy (including DEA number), the specific product prescribed and dispensed, the date the prescription was written, the date the prescription was dispensed, a new

national/health-science/states-require-doctors-to-use-prescription-drug-monitoring-systems-for-patients/2018/01/12/c76807b8-f009-11e7-97bf-bba379b809ab_story html.

311 "About," OARRS, https://www.ohiopmp.gov/About.aspx; Garner Deposition, pp. 126-128.

312 Exceptions to mandatory checks include if the drug is prescribed to a hospice patient or a patient diagnosed as terminally ill; for a duration not to exceed seven days; for the treatment of cancer; for administration in a hospital, nursing home, or residential care facility; or is to treat acute pain resulting from a surgical or other invasive procedure ("Mandatory OARRS Registration and Requests," Ohio BOP, https://www.pharmacy.ohio.gov/Documents/Pubs/Special/OARRS/Mandatory%20OARRS%20Registration%20and%20Requests.pdf; Garner Deposition, pp. 126-129).

313 "State Medical Board Threatens 12,000 Physicians with Being OARRS Non-Compliant," Ohio Academy of Family Physicians, https://www.ohioafp.org/wfmu-article/state-medical-board-threatens-12000-physicians-with-being-oarrs-non-compliant/.

314 "Frequency of Prescription Drug Monitoring Program (PMP) Data Reporting – Map," National Alliance for Model State Drug Laws, January 2, 2019, https://namsdl.org/wp-content/uploads/Frequency-of-Prescription-Drug-Monitoring-Program-PMP-Data-Reporting-Map.pdf.

prescription vs. refill indicator, and the source of payment (i.e., insurance provider and/or cash).[315] Certain states also include overdose rescues, hospitalizations for drug-related conditions and drug-related arrests, and other relevant information from law enforcement.[316]

130. Pharmacists are skilled professionals who provide information to patients on drug risks, drug-to-drug interactions, and the proper use of products.[317] While the prescribing HCP bears responsibility for proper prescribing, I understand that pharmacies have a "corresponding responsibility" to fill prescriptions in accordance with "the usual course of professional treatment".[318]

131. As noted previously in this report, pharmacists now are required to submit information to OARRS regarding controlled substances within one day of dispensing.[319] This information includes the identity of the patient, the prescribing HCP, the date the prescription was dispensed, a new prescription vs. refill indicator, and the source of payment (i.e., insurance provider and/or cash).[320] Pharmacies also have access to OARRS, allowing them to see other controlled substance prescriptions dispensed to their patients by other pharmacies.[321]

---

315 "Prescription Drug Monitoring Programs: Critical Decision Support Tools to Respond to the Opioid Crisis," National Alliance for Model State Drug Laws, https://namsdl.org/wp-content/uploads/Congressional-Briefing-Final-Agenda-and-Presentation.pdf.

316 Vestal 2018.

317 "The Role of the Pharmacist in the Health Care System," WHO, http://apps.who.int/medicinedocs/en/d/Jh2995e/1.6.2 html.

318 21 CFR § 1306.04.

319 "Frequently Asked Questions," OARRS, https://www.ohiopmp.gov/FAQ.aspx. See also Garner Deposition, pp. 141-142. In addition, the DEA requires that pharmacists keep records of all controlled substances that are dispensed as well as inventories for a minimum of two years (https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section4 htm).

320 "Ohio Data Submission Dispenser Guide," Ohio BOP, October 2017, pp. 22-36. https://www.pharmacy.ohio.gov/Documents/Pubs/Special/OARRS/Mandatory%20OARRS%20Registration%20and%20Requests.pdf.

321 "Welcome to OARRS," OARRS, https://www.ohiopmp.gov/. Note that PDMPs typically legally restrict pharmacies from reviewing the information for any patient other than the one presenting a prescription for a covered drug ("OARRS Acceptable Use Policy Pharmacist," Ohio BOP, https://www.ohiopmp.gov/Documents/General/ACCEPTABLE_USE_POLICIES/Acceptable%20Use%20Policy%20(Pharmacist)%20-%20Rules%20regarding%20use%20of%20OARRS%20by%20pharmacists.pdf; Garner Deposition, pp. 172-173).

Pharmacists are required to check OARRS prior to dispensing an outpatient prescription of a controlled substance when the patient adds a new or different controlled substance to their therapy, an OARRS report has not been reviewed for that patient during the preceding twelve months, a prescriber is located outside the usual geographic area, or the pharmacist is suspicious of prescribing patterns or the patient's behavior.[322]

132. Pharmacies have information on only the limited set of transactions with which they are involved. A pharmacy would know the prescriptions that it received for and dispensed to each patient.[323] Individual pharmacies, however, would not be aware of the quantities of drugs delivered to and dispensed by competing pharmacies, except with respect to their own patients if they consulted the PDMP. Further, until December 2017, an Ohio pharmacy would not necessarily have information on the reason or diagnosis supporting an opioid prescription.[324] A pharmacy also would not know whether the drug being dispensed is used as prescribed or otherwise diverted.

133. Under their reporting obligations to the DEA regarding schedule II controlled substances, distributors are required to report transactions to the DEA's Controlled Substance Ordering System ("CSOS") within two days, including identifying the drug sold, the dosage quantity, and the recipient's DEA number.[325] Distributors also are required to submit to the DEA's ARCOS database at least quarterly information on schedule II and III inventories, acquisitions, and distribution, including the name, address, registration number of the person to

---

322 "When to Check OARRS – Pharmacists," Ohio BOP, https://www.pharmacy.ohio.gov/Documents/LawsRules/RuleChanges/OARRSRules/When%20to%20Check%20OARRS%20-%20Pocket%20Card%20-%20Prescribers%20and%20Pharmacists.pdf.

323 Chain pharmacies may have the information for all pharmacies in the chain (Marcum, Zachary A. et al., "Impact of Multiple Pharmacy Use on Medication Adherence and Drug-drug Interactions in Older Adults with Medicare Part D," *Journal of American Geriatric Society*, 62:2, 2014, p. 4).

324 Beginning in December 2017, prescribers were required to include at minimum the first four characters of the ICD-10-CM medical diagnosis code on prescriptions (Ohio Administrative Code 4729-5-30 (B)(14)(a)(i); "E-news Update," Ohio BOP, https://www.pharmacy.ohio.gov/Documents/Pubs/Newsletter/2017/E-News%20Update%20(December%202017).pdf).

325 "Q & A's," DEA Diversion: E-Commerce Program, https://www.deaecom.gov/qanda html; "CSOS EDI Reporting Format," https://www.deaecom.gov/csos_records.pdf.

whom a controlled substance was distributed, and the quantity that was distributed.[326]

134. For Ohio, distributors are also required to report to OARRS wholesale transactions, "suspicious" orders, and customer information. Wholesale transactions must be reported at least once every month, no later than 45 days after the earliest transaction being reported.[327]

135. Distributors know their own purchases from individual manufacturers and their own sales to pharmacy customers. An individual distributor, however, does not know the sales made by other unaffiliated distributors or the direct sales by manufacturers to individual pharmacies. Therefore, any particular distributor would not know the aggregate quantities of drugs being delivered into an individual pharmacy, a county, or other geographic area. Similarly, distributors would not typically know pharmacy dispensing to individual patients.[328] Nonetheless, I understand distributors have at times requested de-identified information on historical dispensing data from prospective customers, and for some actual customers, on a voluntary and ad hoc basis.[329] Similarly, distributors occasionally would inquire about whether prospective customers use other distributors and would conduct on-site visits for red flags.[330]

---

326 21 CFR §§ 1304.21, 1304.33. See also "ARCOS Registrant Handbook," DEA, August 1997, § 1.4.

327 "Instructions for Reporting Wholesale Transactions, Suspicious Orders and Customers to OARRS," Ohio BOP, pp. 1, 3, 4, 6, 10; "FAQ: Suspicious Order Monitoring and Due Diligence," Ohio BOP, April 4, 2019, https://www.pharmacy.ohio.gov/Documents/Pubs/Special/SUSPICIOUS_ORDER/Suspicious%20Order%20Monitoring%20and%20Due%20Diligence.pdf.

328 "What The Washington Post Won't Say About Distributors and Regulation of Controlled Substances in the Supply Chain," Healthcare Distribution Alliance, https://www.hda.org/news/2017-10-15-correcting-the-record?&p=1. After 2015, McKesson's Director of Regulatory Affairs began obtaining three months of anonymized dispensing data for pharmacies, including the specialty of the prescriber (Deposition of Blaine Matthew Snider, Director of Operations, New Castle Distribution Center at McKesson, November 8, 2018 ("Snider Deposition"), pp. 485-486).

329 I understand ABDC, Cardinal, McKesson, H.D. Smith, and Miami-Luken, Inc. have at times requested dispensing data from prospective customers and for ABDC, H.D. Smith, and Cardinal, at times existing customers ("Red Flags and Warning Signs Ignored: Opioid Distribution and Enforcement Concerns in West Virginia," House Energy & Commerce Committee, December 19, 2018 ("E&C 2018"), pp. 113, 117-119).

330 Snider Deposition, pp. 164-178, Exhibit 11.

136. I understand that under their reporting obligations to the DEA for schedule II and III opioids, manufacturers must submit transaction data within two business days to CSOS, including identifying the drug sold, the dosage quantity, and the recipient's DEA number.[331] Manufacturers also are required to submit to the DEA's ARCOS database at least quarterly information on schedule II and III inventories, manufacturing, acquisitions, and distribution, including the name, address, and registration number of the person to whom a controlled substance was distributed, and the quantity that was distributed.[332] Manufacturers have identical responsibilities as distributors regarding reporting to OARRS.[333]

137. Manufacturers have information regarding the sales of their own products to distributors, the sales that they make direct to retail pharmacies, and the sales that they make to other direct purchasers. To the extent a manufacturer has an inventory management agreement ("IMA") with a specific distributor, it may receive information on the inventory levels of its products at the distributor.[334] To the extent that the manufacturer has a chargeback agreement with respect to a purchaser, the manufacturer also would have data on the sales that distributors make to that purchaser. To the extent that a manufacturer has a rebate agreement with a TPP, the manufacturer will receive information from the TPP, typically

---

331 "Q & A's," DEA Diversion: E-Commerce Program, https://www.deaecom.gov/qanda html; "CSOS EDI Reporting Format," https://www.deaecom.gov/csos_records.pdf.

332 21 CFR §§ 1304.21, 1304.33. See also "ARCOS Registrant Handbook," DEA, August 1997, § 1.4.

333 "FAQ: Suspicious Order Monitoring and Due Diligence," Ohio BOP, April 4, 2019, https://www.pharmacy.ohio.gov/Documents/Pubs/Special/SUSPICIOUS_ORDER/Suspicious%20Order%20Monitoring%20and%20Due%20Diligence.pdf; "Instructions for Reporting Wholesale Transactions, Suspicious Orders and Customers to OARRS," Ohio Board of Pharmacy, March 27, 2019, https://www.ohiopmp.gov/Documents/General/WHOLESALE_DISTRIBUTORS/Instructions%20for%20Reporting%20Wholesale%20Transactions,%20Suspicious%20Orders%20and%20Customers%20to%20OARRS.pdf.

334 Manufacturers and distributors may enter into IMAs whereby distributors provide manufacturers with inventory data on the manufacturer's own products at regular intervals ("How can pharmaceutical and life sciences companies monitor their wholesalers to minimize financial losses and distribution risks?," PWC, 2015, https://www.pwc.com/gx/en/pharma-life-sciences/pdf/pwc-pharma-wholesaler.pdf). For example, Purdue Pharma L.P. had fee-for-service agreements to see data at the retail level (Deposition of Stephen Seid, Former Director of National Accounts at Purdue, December 12-13, 2018, pp. 81-82, 137-138, 144-145.

quarterly, on the volume of product that was reimbursed by the TPP.[335] Typically, manufacturers do not receive information about individual prescriptions or patients, other than to the extent they provide patients assistance with coverage, copay discounts, or indigent care.

138. Manufacturers do not have information regarding the sales and shipments of other manufacturers' products. To the extent such information is available, it must be purchased from data companies such as IQVIA (formerly known as IMS Health). These data are collected by IQVIA from participating manufacturers, wholesalers, and pharmacies.[336] IQVIA uses statistical analysis to project sales at the national level.[337] The sales data are often available weekly, typically the week following. Manufacturers also may purchase information from IQVIA and other data companies regarding estimates of the prescribing behavior of individual physicians.[338]

139. I understand that Distributors did not have access to data from IQVIA or its predecessors showing purchases of specific NDCs or opioid molecules at the individual pharmacy level. Furthermore, it appears IQVIA may not even be able to provide such comprehensive data to Distributors.[339]

140. Finally, TPPs have access to information through the claims that are processed, such as retail pharmaceuticals dispensed, the prescribing physicians, and other

---

335 To the extent that a contract with a TPP was based on a product's share of a therapeutic category reimbursed by a TPP, then the manufacturer will also have information on the volume of prescriptions of competing products that were reimbursed by a TPP.

336 "Sales Information," https://www.iqvia.com/locations/united-states/commercial-operations/essential-information/sales-information; "DDD Outlet Subcategory Codes," IQVIA, January 2018.

337 "HSRN Data Brief: National Sales Perspectives," IMS Institute for Healthcare Informatics, 2011. For example, IQVIA's Xponent audit is based on a sample of approximately 50,000 retail pharmacies ("U.S. Opioid Prescribing Rate Maps," Centers for Disease Control and Prevention, https://www.cdc.gov/drugoverdose/maps/rxrate-maps html).

338 See e.g., ALLERGAN_MDL_02949563-564.

339 For example, IQVIA may have restrictions on how it can use a pharmacy's data, limiting its ability to provide a specific pharmacy's non-anonymized data to clients (see CVS-MDLT1-000119346-362 at 346-347). Distributors also may have restrictions on providing pharmacies' ordering data to IQVIA (see WMT_MDL_000058949-9000 at 8966).

information.[340] I understand, however, that TPPs have no reporting requirements to the DEA or OARRS. In certain circumstances (e.g., prior approval requirements), TPPs learn the diagnosis associated with a prescription. Accordingly, TPPs have information on both the history of dispensing to a patient, provided the patient chooses to process the prescription through the TPP, and may have access to a large sample of a physician's prescribing, to the extent that a large percentage of the physician's patients use the TPP for their prescription benefits. In this regard, for example, state Medicaid agencies, such as Ohio Medicaid, are aware of all opioids that were dispensed to state Medicaid recipients, to the extent that the state Medicaid recipients processed their opioid prescriptions through state Medicaid.[341] Similarly, Ohio Medicaid was aware of the physicians who were prescribing opioids to its recipients.

141. Individual TPPs, however, do not know what prescriptions a physician is writing for patients that do not use the TPP to process their prescription benefits and do not know how many opioids are being dispensed in a community to the extent that those opioids prescriptions are being processed by other TPPs or by other means, such as cash payment. Further, the TPP does not know what a patient does with a drug after it is dispensed, whether it is taken as prescribed, or whether the patient diverts the product.

(b) Information Available to Other Key Parties

142. In contrast to the physicians, pharmacies, distributors, manufacturers, and TPPs discussed above, there are government agencies who had all of the information required to identify diversion, had that information on a timely basis, and had the

340 "The Prescription Opioid Epidemic: An Evidence Based Approach," Johns Hopkins Bloomberg School of Public Health, https://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/research/prescription-opioids/JHSPH_OPIOID_EPIDEMIC_REPORT.pdf, p. 32.

341 Further, ODM receives access to OARRS reports for Medicaid beneficiaries ("OARRS Acceptable Use Policy: Ohio Department of Medicaid," https://www.ohiopmp.gov/Documents.aspx).

ability to enforce corrective and sustaining action. I begin by considering the DEA.

143. First, as discussed earlier in this report, the DEA sets the quota that governs the production of all scheduled products. As shown in Exhibits III-6 and III-7, the APQs for oxycodone and hydrocodone were generally increasing from 2006 to 2013.

144. Second, in connection with its activities, the DEA collects and analyzes data on all shipments of controlled substances. The CSA requires any party who "manufacturers, distributes, dispenses," or conducts research involving controlled substances, to register with the DEA, "unless they are exempt."[342] The CSA mandates that registrants report to the DEA all transactions related to the shipment of controlled substances. Information is typically submitted to the DEA through the ARCOS Electronic Data Interchange ("EDI") reporting system.[343]

> ARCOS is a system [...] which monitors the flow of DEA controlled substances from their point of manufacture through commercial distribution channels. [...] ARCOS accumulates these transactions which are then summarized into reports which give investigators in Federal and state government agencies information which can then be used to identify the diversion of controlled substances into illicit channels of distribution.[344]

145. Thus, from the pharmaceutical ingredient manufacturing stage, through secondary manufacturing, through shipping of manufactured products to distributors

---

342 21 U.S.C. § 822(a); "Legal Authorities Under the Controlled Substances Act to Combat the Opioid Crisis," Congressional Research Service, December 18, 2018, ("CRS Report, 2018"), p. 9. Exemptions from the CSA's regulatory requirements include: (i) federal officers or employees "authorized to possess, import, or export controlled substances in the course of their official duties" such as those from the DEA, the U.S. Customs Service, or the FDA; (ii) officers or employees of the state or political sub-departments of the state whose official duties include enforcing laws related to controlled substances; and (iii) a person "who [legally] possesses … a controlled substance for his own legitimate medical use" (CRS Report, 2018, p.10; 21 CFR 1301.22-1301.24 (1997)).

343 "ARCOS Registrant Handbook," DEA, https://www.deadiversion.usdoj.gov/arcos/handbook/full.pdf.

344 "Automation of Reports and Consolidated Orders System (ARCOS)," DEA, https://www.deadiversion.usdoj.gov/arcos/index html.

(including self-warehousing pharmacies) and by those distributors, the DEA receives shipment data, including quantities and recipients with a delay of no longer than every two business days.[345] The DEA also requires at least quarterly inventories of product at each stage of the supply chain and information on any thefts within one business day of discovery.[346] As such, through ARCOS, the DEA has detailed records concerning which products were delivered to which pharmacies, individually and in the aggregate. Further, pharmacies and other entities that dispense product must keep records available to the DEA on their dispensing of controlled substances.[347]

146. For the period at issue, only the DEA had access to the full ARCOS database.[348] The DEA releases an annual publication detailing total opioid shipments (in grams) for each of the previous four quarters, by ingredient and by 3-digit zip code level.[349] The aggregated data are publically available, but typically not until the following year.[350]

147. Until recently, these reports were the only ARCOS data available to distributors beyond their own data. In February 2018, however, the DEA made available a tool providing manufacturers and distributors information on the number of manufacturers and wholesalers through which a prospective customer has purchased a controlled substance from in the past six months. The amount of

345 "Q & A's," DEA Diversion: E-Commerce Program, https://www.deaecom.gov/qanda html; "CSOS EDI Reporting Format," https://www.deaecom.gov/csos_records.pdf.

346 21 CFR 1304.33(b); 21 CFR 1304.33(e); "Theft/Loss Reporting," DEA, https://www.deadiversion.usdoj.gov/21cfr_reports/theft/index.html.

347 21 CFR 1304.05(a).

348 Gray, John, "Responses to Questions for the Record," U.S. Senate Committee on the Judiciary Hearing "Oversight on the Ensuring Patient Access and Drug Enforcement Act," December 20, 2017, pp. 1-3.

349 "ARCOS Retail Drug Summary Reports," DEA, https://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index html.

350 For example, the run date on the 2017 ARCOS Retail Drug Summary Report was July 3, 2018; the run date on the 2016 ARCOS Retail Drug Summary Report was February 3, 2017 ("ARCOS Retail Drug Summary Reports," DEA, https://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index html).

product purchased, though, was information that was not made available.[351] Then, in October 2018, the "Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act" was established, requiring the DEA to provide manufacturers and distributors with anonymized data collected through ARCOS on a more timely basis. Accordingly, as of February 2019, manufacturers and distributors have the capability to "view and download the number of distributors and the amount (anonymized data in both grams and dosage units) each distributor sold to a prospective pharmacy customer in the last available six months of data."[352]

148. Thus, by contrast to the Distributors, who were aware only of the opioids that they delivered to particular pharmacy customers, the DEA, through the CSOS submissions and the ARCOS database, had a complete and aggregate picture of all deliveries of all controlled substances to all pharmacies within the Counties for the entirety of the relevant time period. Additionally, as discussed earlier in this report, the DEA had the regulatory authority to take any and all action that might be warranted to stop diversion revealed by the CSOS submissions and the ARCOS data.

149. With respect to Ohio, the Ohio BOP collected data on opioid prescribing through OARRS, its PDMP program. In addition, the Ohio WCB has access to Rx History Reports data on a patient-by-patient basis through OARRS. As a result, the Ohio WCB also was aware of the opioids prescribed and dispensed to its claimants, to the extent that opioid prescriptions were processed through the WCB. In contrast, other private insurers were not able to access patient data through OARRS.[353]

---

351 "DEA Creates New Resource To Help Distributors Avoid Oversupplying Opioids," DEA Media Release, February 14, 2018, https://www.dea.gov/press-releases/2018/02/14/dea-creates-new-resource-help-distributors-avoid-oversupplying-opioids).

352 "DEA announces enhanced tool for registered drug manufacturers and distributors to combat opioid crisis," DEA Media Release, February 26, 2019, https://www.dea.gov/press-releases/2019/02/26/dea-announces-enhanced-tool-registered-drug-manufacturers-and.

353 Garner Deposition, pp. 98-99; "OARRS Acceptable Use Policy Ohio Department of Medicaid," Ohio BOP, https://www.ohiopmp.gov/Documents/General/ACCEPTABLE_USE_POLICIES/

150. Through OARRS, the Ohio BOP is able to trace a drug dispensed to a patient, to the pharmacy that dispensed the drug, and the manufacturer who produced the drug through the NDC code.[354] The Ohio BOP uses data collected from OARRS to run analyses and publish reports looking for potential crime as well as identifying individuals who may be at risk.[355]

(a) The Ohio BOP runs reports at the patient level, seeking to identify diversion through doctor shopping and overutilization.[356] Reports also are run to analyze the number of prescriptions and the pharmacies from which a particular patient is obtaining a medication.[357] Accordingly, the Ohio BOP had the ability to flag and identify these sources of diversion at the patient level.

(b) The Ohio BOP also runs reports on the prescriber side. OARRS receives a list of individuals who died from an overdose from the Ohio Department of Health, permitting an assessment of prescribers with high rates of overdose.[358] The Ohio BOP runs reports on purchase quantity by prescribers to determine if these purchase quantities are higher than the quantities that these physicians are permitted to dispense.[359] The Ohio BOP runs reports on the "overprescribing"[360] of specific drugs or

---

Acceptable%20Use%20Policy%20(Medicaid)%20-%20Rules%20regarding%20use%20of%20OARRS%20by%20the%20Ohio%20Department%20of%20Medicaid.pdf; "OARRS Acceptable Use Policy Ohio Bureau of Workers' Compensation," Ohio BOP, https://www.ohiopmp.gov/Documents/General/ACCEPTABLE_USE_POLICIES/Acceptable%20Use%20Policy%20(BWC)%20-%20Rules%20regarding%20use%20of%20OARRS%20by%20the%20Ohio%20Bureau%20of%20Workers%20Compensation.pdf.

354 If a pharmacy orders the same drug from multiple distributors, OARRS is not able to trace the exact prescription to the exact distributor (Garner Deposition, pp. 157-158).

355 Garner Deposition, pp. 62-63.

356 Garner Deposition, p. 138.

357 These reports can also be run ad hoc (Garner Deposition, p. 87).

358 I understand that these reports were provided to OARRS on an annual basis (Garner Deposition, pp. 199-200). To the extent that the state believed it appropriate for OARRS to receive these reports on a more timely basis, I am not aware of any reason why that was not done.

359 Office-based physicians in Ohio are permitted to administer office-based opioid treatment to no more than 30 patients (Ohio Revised Code, Title 47, Chapter 4729.553).

360 Note that it is not apparent how the Ohio BOP defines "overprescribing".

combinations of drugs, dispensing patterns, and the prescribing of combinations of drugs that are deemed to be risky.[361] Accordingly, the Ohio BOP had the ability to identify instances of overprescribing by physicians.

(c) The Ohio BOP also creates reports which show county-level opioid dispensing in MME per capita and per patient, the number of opioid prescriptions per capita and per patient, and the number of prescriptions dispensed in each county by major drug classes.[362] Accordingly, the Ohio BOP has the ability to identify instances of overprescribing and diversion at the patient and county level.

151. Thus, in contrast to Distributors, who were aware only of the opioids that they delivered to particular pharmacy customers, the Ohio BOP, through the OARRS database, had complete information regarding all prescriptions written and dispensed for all controlled substances written by all physicians for all Ohio patients.[363] Unlike Distributors, the Ohio BOP, by way of example, had the ability to identify high-prescribing doctors, high-dispensing pharmacies, and individuals being prescribed and dispensed high doses and quantities of prescription opioids. Additionally, the Ohio BOP, in conjunction with the Ohio SMB, had the regulatory authority to take any and all action that might be warranted to stop diversion revealed by the OARRS data.

---

361 Garner Deposition, pp. 81-84, 87. See also Deposition of Allisyn Leppla, Former Injury Prevention Coordinator, Cuyahoga County Board of Health, January 15, 2019 ("Leppla Deposition"), pp. 58-59, noting "The OARRS system [is] helpful because it allowed individuals to monitor prescribing trends and prescribing patterns, overprescribing by specific physicians, as well as for individuals that potentially would have been what was considered doctor shopping."

362 Garner Deposition, pp. 72-74. See also Leppla Deposition, pp. 58-59.

363 Ohio law requires prescribers who practice primarily in an Ohio county that adjoins another state to request the adjoining state's prescription drug information through OARRS prior to prescribing. Ohio is one of 47 states that is legally authorized to share their PDMP data with other state jurisdictions ("Mandatory OARRS Registration and Requests," Ohio BOP, https://www.pharmacy.ohio.gov/Documents/Pubs/Special/OARRS/Mandatory%20OARRS%20Registration%20and%20Requests.pdf; "Interjurisdictional Sharing of Prescription Drug Monitoring Program (PMP) Data – Ma," National Alliance for Model State Drug Laws, https://namsdl.org/wp-content/uploads/Interjurisdictional-Sharing-of-Prescription-Drug-Monitoring-Program-PMP-Data-Map.pdf).

V. OVERVIEW OF SUBSTANCE ABUSE

152. Plaintiffs assert that the availability of prescription opioids through the pharmacy channel has been the cause of addiction, monetary damages, and death. Substance abuse, however, has been a scourge in the U.S. for decades. The consequences of addiction, damages, and death are not new. It was not the availability of prescription opioids from pharmacies that led to these issues in the past. The factors that drove substance abuse in the past persist today.

A. Opioids and Other Drugs of Abuse in the U.S.

153. The modern history of opioids began in the late eighteenth / early nineteenth century, when a German pharmacist discovered morphine by pouring liquid ammonia over opium and noted that the resulting substance was much more powerful than opium. Articles published in scientific journals in the early nineteenth century encouraged the widespread use of morphine by doctors. The use of morphine grew further over the course of the nineteenth century as additional medical results were published.[364] Between the U.S. Civil War and 1914, the number of Americans using opiates increased significantly. Opiates, including morphine and heroin, were readily available in the U.S. until 1914.[365]

154. Heroin is a highly addictive opioid, sold in various forms.[366] Since the early twentieth century there have been three main periods in which heroin abuse was relatively prevalent in the U.S.:

(a) Following World War II, with the highest incidence occurring in the late 1940s and early 1950s;[367]

---

364 Abadinsky, Howard, *Drug Use and Abuse: A Comprehensive Introduction*, 9th Edition, Cengage Learning, 2018, ("Abadinsky 2018"), p. 24.

365 Abadinsky 2018, p. 25.

366 2018 National Drug Threat Assessment, DEA, October 2018, ("2018 National Drug Threat Assessment"), https://www.dea.gov/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20final%20low%20resolution.pdf, p. 11.

367 Hughes, P.H. and O. Rieche, "Heroin Epidemics Revisited," *Epidemiologic Reviews*, 17:1, 1995, ("Hughes and Rieche 1995"), p. 66.

(b) Starting in the late 1960s, with the highest incidence occurring between 1971 and 1977;[368] and

(c) From approximately 2007 to the present.[369]

155. In addition to opioids, other substances have a long history of use and abuse.[370]

(a) Throughout American history, governments have attempted to curb alcohol use and establish treatment programs for alcohol abuse.[371]

(b) After cocaine was added to a variety of OTC items in the early 1900s, widespread use ensued; by the 1920s, cocaine was the most feared of all illicit drugs.[372] Following a surge of use in the 1970s, cocaine abuse had reached "pandemic proportions".[373] After a decline in popularity, its use appears to be rising once more.[374]

(c) In 1932, amphetamines became available and were a cheaper legal alternative to cocaine; abuse began almost immediately.[375] The production of methamphetamine in small operations, known as "meth labs", began in California in the 1950s.[376] Methamphetamine use has

368 Hughes and Rieche 1995, p. 66.

369 2018 National Drug Threat Assessment, pp. 11-20; Bauman, Zachary M. et al., "The Heroin Epidemic in America: A Surgeon's Perspective," *Surgical Infections*, 20, 2019.

370 Deposition of James A. Gutierrez, Cuyahoga County Prosecutor, Economic Crimes Unit, January 31, 2019, p. 61.

371 See, for example, Brown, Lawrence S. Jr., "Substance Abuse and America: Historical Perspective on the Federal Response to a Social Phenomenon," *Journal of the National Medical Association*, 73:6, 1981, ("Brown 1981").

372 Das, Gopal, "Cocaine Abuse in North America: A Milestone in History," *Journal of Clinical Pharmacology*, 33, 1993, ("Das 1993"), pp. 297-298.

373 "Cocaine: A Major Drug Issue of the Seventies," Hearing before the Select Committee on Narcotics Abuse and Control, House of Representatives, Ninety-sixth Congress, First Session, July 24, 26, October 10, 1979, ("Congressional Hearings 1979"), p. 1.

374 2018 National Drug Threat Assessment, pp. 39-57. See also Kariisa, Mbabazi et al., Drug Overdose Deaths Involving Cocaine and Psychostimulants with Abuse Potential – United States, 2003-2017, *Morbidity and Mortality Weekly Report*, 68:17, May 3, 2019, pp. 388-395.

375 Abadinsky 2018, p. 40; Gahlinger, Paul, *Illegal Drugs A Complete Guide to Their History, Chemistry, Use, and Abuse*, 2004, ("Gahlinger 2004"), p. 206.

376 Gahlinger 2004, p. 213.

increased significantly since the 1990s and in 2015 was reported to be the second most widely misused substance, following cannabis.[377]

B. U.S. Government Efforts to Counter Drug Abuse

156. Government efforts to curb the use of addictive substances also have a long history. For example, the Harrison Anti-Narcotics Act of 1914 ("Harrison Act") required any person in the business of selling certain drugs, including opium derivatives and cocaine, to register and pay a tax annually. The Harrison Act made it illegal to sell or give away opium or its derivatives and coca or its derivatives without permission from the Commissioner of Revenue.[378] Amendments to the Harrison Act in 1922 and 1924 imposed federal penalties and extended a prohibition on the importation and use of opium and cocaine for non-medicinal purposes to include coca leaves, opium derivatives, and the importation of heroin.[379]

157. In 1951, amphetamine abuse became a major concern and the Harrison Act was amended to require prison sentences for offenders. In response to the continued proliferation of amphetamines, the Narcotics Manufacturing Act of 1960 and the Racketeer Influenced Corrupt Organizations Act ("RICO") of 1962 were used to target racketeering and organized crime in the amphetamine trade.[380] In the 1960s, abuse of hallucinogens and amphetamines increased.[381] The President's Commission on Narcotics and Drug Abuse advocated approaches viewing illicit drug abuse as a disease, leading to the establishment of federally funded community mental health centers.[382]

---

377 Galbraith, Niall, "The methamphetamine problem," *BJPsych Bulletin*, 39, 2015, p. 218.

378 Abadinsky 2018, p. 31.

379 Brown 1981, p. 501.

380 Gahlinger 2004, p. 63.

381 Abadinsky 2018, pp. 43-46.

382 Musto, David F., "Drug Abuse Research in Historical Perspective," *Pathways of Addiction: Opportunities in Drug Abuse Research*, Institute of Medicine (US) Committee on Opportunities in Drug Abuse Research, 1996, ("Musto 1996"), https://www ncbi nlm nih.gov/books/NBK232965/.

158. In 1970, Congress passed the Comprehensive Drug Abuse Prevention and Control Act ("CDAPCA"). Title II of the CDAPCA includes the CSA. The CDAPCA established for the first time in the U.S. a single system for the control of both narcotic and psychotropic drugs. It also established the current classification of controlled substances based on varying levels of harm (i.e., potential for abuse and addiction) and legitimate medical use.[383]

159. President Nixon declared drugs "public enemy number one" at a press conference in June 1971, initiating the "war on drugs" in the U.S.[384] In 1973, the DEA was created by executive order and charged with development and maintenance of a National Narcotics Intelligence system in cooperation with federal, state, and local officials.[385]

160. Between July and October 1979, a Congressional Select Committee on Narcotics Abuse and Control held a series of hearings to discuss the worsening cocaine epidemic in the United States.[386] The following year, Congress allocated funds for use in prevention and education activities in drug abuse.[387]

161. In the 1980s, motivated to a large degree by the perceived widespread use of crack cocaine, President Reagan reinforced and expanded many of President Nixon's war-on-drugs-related policies. In 1984 and 1986, Congress passed the Federal Sentencing Reform Act and the Anti-Drug Abuse Act, which re-established mandatory minimum prison sentences for certain drug offenses, with the latter expanding to cocaine-related charges.[388] President Reagan's war on

---

383 Gahlinger 2004, pp. 63-64; Musto 1996; "The DEA Years," DEA, https://www.dea.gov/sites/default/files/2018-07/1970-1975%20p%2030-39.pdf, ("The DEA Years"), p. 31.

384 Barber, Chris, "Public Enemy Number One: A Pragmatic Approach to America's Drug Problem," Richard Nixon Foundation, June 29, 2016, https://www.nixonfoundation.org/2016/06/26404/.

385 The DEA Years, pp. 30-39.

386 Congressional Hearings 1979.

387 "Increased Heroin Supply and Decreased Federal Funds: Impact on Enforcement, Prevention, and Treatment," A Report of the Select Committee on Narcotics Abuse and Control, Ninety-sixth Congress, Second Session, 1980, ("Congressional Hearings 1980"), p. 1.

388 Clark, Claire D., *The Recovery Revolution*, 2017, ("Clark 2017"), pp. 157-159; Gahlinger 2004, pp. 65-67; Anti-Drug Abuse Act of 1986, Pub. L. No. 99-570.

drugs policies focused on drug supply; of the increased budget to combat drugs, 70 percent was allocated to stop drugs at the source and 30 percent was dedicated to education, prevention, and treatment of drug users.[389]

162. In recent decades, public support for the war on drugs has declined. Nonetheless, the DEA reports that drug use remains prevalent and that drug poisoning deaths are the leading cause of injury deaths in the U.S.[390] National survey data show that more than two-thirds of Americans want the government to focus on treatment based approaches to illegal drug use in lieu of prosecuting.[391] In 2010, Congress passed the Fair Sentencing Act, which reduced or eliminated mandatory minimum sentences for certain drug offenses.[392]

C. Factors Predicting Substance Abuse

163. In broad terms, I understand Plaintiffs allege that Distributors' deliveries and alleged failures to report and block deliveries caused or facilitated addiction to prescription opioids, leading to addiction to illicit opioids that, in turn, gave rise to economic and societal harms requiring expenditures by the Counties.[393] The causal chain that Plaintiffs assert, however, is incomplete and does not properly account for the history, incidence, and prevalence of drug abuse in the U.S. Nor is it apparent that Plaintiffs consider and account for the highly effective analgesic properties of prescription opioids and the quality of life improvements, costs saved, economic value of those able to return to work, and lives saved from unremitting and excruciating pain that are the result of appropriately prescribing and using opioids effectively for pain treatment,

---

389 Gahlinger 2004, p. 66.

390 2018 National Drug Threat Assessment.

391 According to the Pew Research Center, 40 states took action to ease their drug laws between 2009 and 2013 ("America's New Drug Policy Landscape," Pew Research Center, April 2, 2014, http://www.people-press.org/2014/04/02/americas-new-drug-policy-landscape/).

392 Fair Sentencing Act of 2010, Pub. L. No. 111-220.

393 Cuyahoga Complaint, ¶¶ 14-19; Summit Complaint, ¶¶ 14-20.

164. With respect to claims regarding opioid misuse, abuse, dependence, and addiction, I understand the following terminology is relevant.

(a) Opioid misuse is considered to be synonymous with the non-medical use of prescription opioids, irrespective of whether such use is harmful.[394]

(b) Opioid use disorder is characterized by the improper use of prescription opioids with serious consequences in the individual's ability to function. Opioid use disorder may include dependence and/or abuse.[395] Opioid abuse is characterized by the purposeful use of opioids to obtain particular effects (e.g., a "high").[396] Opioid abuse may be accompanied by administration contrary to the approved dosage, such as crushing pills followed by insufflation or injection.

(c) Addiction lacks a precise clinical definition. The American Academy of Pain Management, the American Pain Society, and the American Society of Addiction Medicine have developed a consensus definition of addiction as "a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving."[397] Medical literature over the past 15 years distinguishes addiction from physical dependence and tolerance.[398] Addiction is understood to be a chronic relapsing disorder in which

394 "Misuse of Prescription Drugs," NIH, https://www.drugabuse.gov/publications/misuse-prescription-drugs/overview.

395 O'Malley, Gerald F. and Rika O'Malley, "Opioid Use Disorder and Rehabilitation," Merck Manual – Professional Version, https://www merckmanuals.com/en-ca/professional/special-subjects/recreational-drugs-and-intoxicants/opioid-use-disorder-and-rehabilitation.

396 Savage et al. 2003, p. 663.

397 Savage et al. 2003, p. 662.

398 Savage et al. 2003, pp. 656-658.

compulsive drug-seeking and drug-taking behavior persists despite serious negative consequences.[399]

165. The literature discusses multiple categories of factors predictive of substance use and abuse in general, including genetics, environmental influences, and mental disorders. Family and twin epidemiological studies show that genes contribute to the vulnerability to addictive disease, with studies finding heritability (i.e. a genetic influence) of 30 to 60 percent.[400] Studies of twins demonstrate that predisposition to addiction may be due to genetic variants that are common to all addictions and, to a more limited degree, due to genetic factors that are specific to a particular drug.[401]

166. Mental disorders have been found to be highly correlated with substance abuse.[402] One frequently-cited study determined that at least one mental disorder excluding alcohol or other drug abuse/dependence has occurred in the lifetime of 22.5 percent of the U.S. population. Among this population, alcohol and other drug abuse-dependence disorders are substantially more common than among the rest of the population: 22.3 percent had a lifetime history of alcohol abuse-dependence and 14.7 percent had a lifetime history of other drug abuse-dependence; among those with no history of mental disorder, the rate of alcohol

---

399 "Drugs, Brains, and Behavior: The Science of Addiction," National Institute of Drug Abuse, https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drug-misuse-addiction. See also Camí, Jordi and Magí Farré, "Drug Addiction," *New England Journal of Medicine*, 349:10, 2003 ("Cami and Farré 2003"), p. 976.

400 Kreek, Mary Jeanne et al., "Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction," *Nature Neuroscience*, 8:11, 2005, ("Kreek et al. 2005"), p. 1450. See also Nielsen, David A et al., "Epigenetics of drug abuse: predisposition or response," *Pharmacogenomics*, 13:10, 2012, p. 2. Heritability ranges from zero to one. Heritability close to zero indicates that almost all of the variability in a trait among people is due to environmental factors, with very little influence from genetic differences ("What is Heritability?," NIH, U.S. National Library of Medicine, April 30, 2019, https://ghr.nlm.nih.gov/primer/inheritance/heritability). Regarding the impact of early childhood trauma, see Deposition of Jeffrey Sturmi, Deputy Chief Probation Officer for the Akron Municipal Court, November 15, 2018, Exhibit 24.

401 Kreek et al. 2005, p. 1450; Kendler, Kenneth S. et al., "Specificity of Genetic and Environmental Risk Factors for Use and Abuse/Dependence of Cannabis, Cocaine, Hallucinogens, Sedatives, Stimulants, and Opiates in Male Twins," *American Journal of Psychiatry*, 160:4, 2003, p. 687.

402 Deposition of Greta Johnson, Summit County Executive's Office Assistant Chief of Staff and Public Information Officer, January 15, 2019, pp. 184-185.

abuse-dependence was 11.0 percent and other drug abuse-dependence was 3.7 percent. Accordingly, a mental disorder in one's lifetime tends to be associated with quadruple the risk of other drug abuse-dependence. The increased risk is statistically significant.[403]

167. Several conditions are associated with an increased risk of a drug abuse diagnosis: bipolar I affective disorder (7.9 times the risk relative to the general population), schizophrenia (6.9 times), antisocial personality disorder (5.2 times), phobias (4.7 times), and obsessive-compulsive disorder (3.2 times). Similarly, substance abuse diagnoses for specific drugs are associated with an increased risk of mental disorders relative to the general population, including cocaine (11.3 times), barbiturates (10.8 times), hallucinogens (8.0 times), opiates (6.7 times), and amphetamines (6.2 times).[404] This correlation between mental disorders and drug abuse has been confirmed by several studies.[405]

168. Additional studies find links between mental health status and overdose death rates, from both illicit drugs and medication. For example, symptoms of depression are associated with higher overdose rates, as is the use of benzodiazepines.[406]

169. Insurance coverage also has been found to be a factor in identifying those who use illicit drugs. Those without health insurance or having only Medicaid coverage

---

403 Regier, Darrel A. et al., "Comorbidity of Mental Disorders With Alcohol and Other Drug Abuse," *Journal of the American Medical Association*, 264, 1990, ("Regier et al. 1990"), pp. 2512-2514. Controlling for age, sex, race / ethnicity, marital status, and socioeconomic status leads to an even higher risk of other drug abuse-dependence among those with a mental disorder (p. 2514).

404 Regier et al. 1990, pp. 2511-2517.

405 See, for example, Kreek et al. 2005, p. 1454; Sullivan, Mark D. et al., "Risks for Possible and Probable Opioid Misuse Among Recipients of Chronic Opioid Therapy in Commercial and Medicaid Insurance Plans: the TROUP Study," *Pain*, 150:2, 2010, pp. 332-339; Rice, J.B. et al., "A Model to Identify Patients at Risk for Prescription Opioid Abuse, Dependence, and Misuse," *Pain Medicine*, 13, 2012, ("Rice et al. 2012"), pp. 1162-1173; White, Alan G. et al., "Analytic Models to Identify Patients at Risk for Prescription Opioid Abuse," *American Journal of Managed Care*, 15:12, 2009, pp. 897-908.

406 Bohnert, Amy S.B. and Mark A. Ilgen, "Understanding Links among Opioid Use, Overdose, and Suicide," *New England Journal of Medicine*, 380:1, 2019 ("Bohnert and Ilgen 2019"), p. 74.

are more likely to abuse or become dependent on heroin than those with other forms of health insurance.[407]

D. Prescription Opioid Misuse and Opioid Use Disorder

170. The frequency of prescription opioid misuse is often reported as a fraction of the overall population. For example, recent research indicates that the rate of past-year non-medical use of prescription opioids was 43.3 per 1,000 persons aged 12 years and older in 2012-2014. This represents a statistically significant decline in the rate of non-medical use from a level of 48.4 per 1,000 in 2003-2005. Rates of non-medical use were highest among males and those aged 18-25; those with low levels of household income and the uninsured also tended to have higher rates of non-medical use. Additionally, past year users of other substances, including marijuana, cocaine, heroin, sedatives, and stimulants, are found to have rates of prescription opioid non-medical use significantly higher than the population average.[408] The same study reports on average rates of prescription opioid abuse and dependence controlling for various factors, concluding:

> Compared to their respective reference groups, the following groups had [statistically significant] higher odds of past-year opioid analgesic abuse or dependence: 18-25 year olds, 26-34 year olds, non-Hispanic whites, people with an annual household income $<20,000 and between $20,000-$49,999, the uninsured, people with Medicaid, and people with substance abuse or dependence on alcohol, marijuana, cocaine, heroin, prescription sedatives or tranquilizers, or prescription stimulants.[409]

171. Rates of misuse in the aggregate population, however, do not directly address the frequency of problematic opioid use among those actually prescribed opioids. This is a relevant issue as it appears that only a minority of prescription opioid misuse arises from the patient's own prescription. According to one interpretation

---

407 Compton, Wilson M. et al., "Relationship between Nonmedical Prescription-Opioid Use and Heroin Use," *New England Journal of Medicine*, 374:2, 2016 ("Compton et al. 2016"), p. 159.

408 Jones, Christopher M., "The paradox of decreasing nonmedical opioid analgesic use and increasing abuse or dependence – An assessment of demographic and substance abuse trends, United States, 2003-2014," *Addictive Behaviors*, 65, 2017, ("Jones 2017"), p. 231.

409 Jones 2017, p. 233.

of the data, "<25% of nonmedical prescription opioid users obtain these drugs from a prescriber; the rest obtain them from friends, relatives, or dealers."[410] Another study, based on survey data from 2015, indicates that among those reporting misuse of prescription opioids in 2015, 59.9 percent used them without a prescription, 22.2 percent used them in greater amounts than directed on the prescription, 14.6 percent used them more often than directed, and 13.1 percent used them for longer than directed.[411] The most common motivation for misuse cited by respondents was to relieve physical pain; this was the case for those with and without an opioid use disorder.[412]

172. Rates of prescription opioid misuse among those receiving opioid treatment have been reported in the literature, with one review reporting average prevalence rates of misuse of 21 to 29 percent among those treated for chronic pain.[413] A recent meta-analysis found that "4.7% of patients prescribed opioid analgesic therapy were associated with *de novo* diagnostic status for opioid dependence or abuse during the follow-up observation period."[414]

---

410 Singer, Jeffrey A. et al., "Today's nonmedical opioid users are not yesterday's patients; implications of data indicating stable rates of nonmedical use and pain reliever use disorder," *Journal of Pain Research*, 12, 2019, ("Singer et al. 2019"), p. 618.

411 Han, Beth, et al., "Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health," *Annals of Internal Medicine*, 167:5, 2017, ("Han et al. 2017"), p. 296.

412 Han et al. 2017, pp. 298-299.

413 Vowles, Kevin E. et al., "Rates of opioid misuse, abuse, and addiction in chronic pain: A systematic review and synthesis," *Pain*, 156:4, 2015, ("Vowles et al. 2015"), p. 569.

414 Higgins, C. et al., "Incidence of iatrogenic opioid dependence or abuse in patients with pain who were exposed to opioid analgesic therapy: a systematic review and meta-analysis," *British Journal of Anaesthesia*, 120:6, 2018, ("Higgins et al. 2018"), pp. 1336, 1339. The study addresses the incidence of diagnosed opioid dependence and abuse, thereby "ensuring examination of debilitating problematic opioid use rather than focusing on aberrant drug-related behavior indiscriminately, which may include recreational use and other forms of non-problematic use (Higgins et al. 2018, p. 1341).

VI. DIVERSION AND ITS DETECTION

A. Introduction

173. I understand that diversion occurs when controlled pharmaceuticals are transferred from "a lawful to an unlawful channel of distribution or use."[415] Examples of diversion cited by the DEA include: "physicians who sell prescriptions to drug dealers or abusers; pharmacists who falsify records and subsequently sell the drugs; employees who steal from inventory and falsify orders to cover illicit sales; prescription forgers; and individuals who commit armed robbery of pharmacies and drug distributors."[416]

174. There are different mechanisms through which controlled pharmaceuticals are "diverted from their lawful purpose into illicit drug traffic."[417] One nationwide survey of individuals receiving treatment for prescription opioid abuse found that 62 percent of respondents obtained prescription opioids from a dealer, 55 percent obtained prescription opioids from sharing or trading with friends and family, 52 percent obtained prescription opioids from a source working in a medical practice, and 18 percent obtained them via theft.[418] Another study examines respondents in the National Survey of Drug Use and Health ("NSDUH") who report misusing a prescription analgesic at least once within the past year. The results of that study show that 55 percent of misusers say they received the drugs from a friend or family member, 11 percent bought or took the drugs from a friend or family member, 5 percent stole them from a friend or family member, 4 percent purchased from a drug dealer, and 0.4 percent said they purchased using the

---

415 Rigg, Khary K., Steven P. Kurtz, and Hilary L. Surratt, "Patterns of Prescription Medication Diversion among Drug Dealers," *Drugs: Education, Prevention and Policy*, 19:2, 2012 ("Rigg et al. 2012"), p. 144.

416 "Diversion Control Division – Program Description," United States Department of Justice ("DOJ") and DEA, https://www.deadiversion.usdoj.gov/prog_dscrpt/index.html.

417 "Diversion Control Division – Program Description," DOJ and DEA, https://www.deadiversion.usdoj.gov/prog_dscrpt/index.html.

418 Cicero, Theodore J. et al., "Multiple Determinants of Specific Modes of Prescription Opioid Diversion," *Journal of Drug Issues*, 41:2, 2011 ("Cicero et al. 2011"), Figure 1. Note that respondents were allowed to select more than one option. Respondents also were allowed to choose a "single" source of prescription opioids; 48 percent indicated "dealer," 20 percent "shared," 28 percent "medical," and 4 percent "theft" (Cicero et al. 2011, Figure 1).

internet; only 17 percent of those who misused a prescription analgesic within the past year had a prescription for the products.[419]

175. In alleging that Distributors failed to meet their responsibility to report certain unusual or "suspicious" orders and/or to block such orders in aid of the DEA's effort to prevent diversion, the Plaintiffs ignore or mischaracterize a number of salient issues.

(a) First, as discussed earlier in this report, while each individual Distributor observes the size and frequency of its own orders and shipments, each individual Distributor does not have full knowledge of the orders and shipments of any other Distributors.

(b) Second, as discussed earlier in this report, other parties have access to more comprehensive information that may be used to identify and prevent diversion in a sustained manner. For example, through ARCOS, the DEA has full information on the orders placed by and shipments to all pharmacies with respect to all distributors and manufacturers. Similarly, PDMPs, such as OARRS in Ohio, have access to prescription-level information including the identity of the prescriber, the identity of the patient, the size of each prescription, and where the prescriptions are being filled. The Distributors lack the comprehensive visibility into interactions between prescribers and patients, patients and pharmacies, and pharmacies and suppliers (either distributors or manufacturers).

(c) Third, any attempt to infer diversion on the basis of the size and frequency of prescription opioid orders placed by pharmacies must address the significant degree of variation in pharmacy ordering that is a natural consequence of the environment. Sources of variation include changes over time in the overall demand for different products as a result of variation in disease incidence and variation and evolution in medical

[419] Manchikanti, Laxmaiah et al., "Opioid Epidemic in the United States," *Pain Physician,* 15:3S, 2012, p. ES22.

practice, changes over time across pharmacies based on demographics and socioeconomic factors, and the natural level of variation that characterizes orders within pharmacies on a month-by-month basis. All of these sources of variation complicate the task of identifying suspected diversion on the basis of pharmacy order size, pattern, and frequency, as I understand is the requirement under the CSA.

(d) Fourth, there is little basis to expect that activities associated with diversion would account for a large volume of opioid prescriptions, making it more difficult to detect diversion. For example, as I show below, "doctor shopping", whereby opioid-seeking patients obtain multiple opioid prescriptions from different HCPs over a short period, accounted for less than 1 percent of opioid prescriptions in the Counties over the period 2008-2017. Similarly, I show below that those physicians cited by the Plaintiffs and/or whose licenses were put on probationary status, suspended, surrendered, or revoked account for at most 10 percent of prescriptions in the Counties over the period 1997-2017.

176. I understand that Distributors have a regulatory obligation to identify orders that "might be indicative of diversion".[420] Nonetheless, Distributors faced the problem of identifying what was expected to be a minority of diverted volumes within overall much larger, legitimate order volumes that were highly variable and that resulted from prescribing decisions made in good faith.[421] Further, it was not Distributors' responsibility to overrule the decisions of the DEA with regard to quotas nor the medical judgment of HCPs. Therefore, I am not aware that Distributors have the obligation (or ability) to assess the volume of prescription

420 MCKMDL00478906-909 at 908.

421 In a 2006 policy statement addressing DEA enforcement with regard to physicians, the DEA indicates "the overwhelming majority of physicians who prescribe controlled substances do so in a legitimate manner that will never warrant scrutiny by Federal or State law enforcement officials. … In any given year, including 2005, fewer than one out of every 10,000 physicians in the United States (less than 0.01 percent) lose their controlled substance registrations based on a DEA investigation of improper prescribing" (71 FR 52715-723 at 719); Testimony of Joseph T. Rannazzasi before the Subcommittee on Commerce, Manufacturing, and Trade of the Committee on Energy and Commerce, House of Representatives, March 1, 2012, p. 94).

opioids ordered by pharmacies in comparison to what may or may not be consistent with medically necessary or appropriate levels for the patients filling prescriptions at those pharmacies.

177. Thus, given the shortcomings in Distributors' information relative to that held by other parties, Distributors' monitoring efforts could have been at most supplementary to the monitoring efforts of better-informed parties, including the DEA, the Ohio BOP, the Ohio SMB, Ohio Medicaid, and Ohio WCB. Further, each of these better-informed parties had the tools and capabilities at their disposal to take more effective and sustained action against diversion.

B. Access to Information on the Signals of Diversion

178. Plaintiffs make several claims regarding types of information that allegedly imply the presence of diversion and to which Distributors allegedly failed to respond. These include allegedly abnormal order levels by pharmacies (and resulting delivery sizes); allegedly abnormal dispensing volumes by pharmacies; and allegedly abnormal prescribing volumes by physicians. For some of these types of information (such as allegedly abnormal dispensing volumes by pharmacies, and allegedly abnormal prescribing volumes by physicians), it is not apparent that Distributors had or could have had any knowledge. For the other types of information (such as allegedly abnormal order levels by pharmacies and resulting delivery sizes), Distributors had inferior information and capabilities to detect and eliminate diversion relative to the DEA, the Ohio BOP, the Ohio SMB, Ohio Medicaid, and Ohio WCB.

(a) Abnormal Order Volumes

179. The Plaintiffs refer to deliveries made by Distributors into Plaintiffs' jurisdictions that "exceeded reasonable medical use."[422] For example, Plaintiffs allege that between 2010 and 2016, Summit County received a per-capita dosage unit average of "623 opioids [per opioid user and] 67 opioids per person per year, both

[422] Summit Complaint, ¶ 689. See also Summit Complaint, ¶¶ 687, 700, and 705.

greater than the already high state average."[423] Plaintiffs go on to state: "[t]he volume of opioids distributed in Summit County is so high as to raise a red flag that not all of the prescriptions being ordered could be for legitimate medical uses."[424]

180. Nonetheless, from 2010 through 2014, the DEA increased the national quota for oxycodone and hydrocodone by 52 percent, on a consolidated MME basis.[425] Between 2010 and 2014, oxycodone and hydrocodone MME per capita shipped into Summit County decreased by 12 percent.[426] Further, as shown on Exhibit VI-1, the relative position of Summit County with respect to oxycodone and hydrocodone shipments per capita in comparison to all counties in the U.S. varied from the [redacted] to [redacted] percentile throughout the period from 2010 through 2014 (and with respect to all opioids, as shown in Exhibit VI-2, from the [redacted] to [redacted] percentile).[427] As such, it is not apparent how such levels of shipments into the Counties could be recognized by Distributors as being "so high as to raise a red flag that not all of the prescriptions being ordered could be for legitimate medical uses."[428] If such were true regarding the level of shipments, it is not apparent why the DEA raised the quotas that allowed such levels of opioids to be produced.

181. Plaintiffs also refer to deliveries made by Distributors to specific pharmacies. For example, Plaintiffs cite HCPs "convicted of crimes involving drug diversion" and that "these individuals, and the pharmacies at which they or their patients filled

---

423 Summit Complaint, ¶ 689; Cuyahoga Complaint, ¶ 639.

424 Summit Complaint, ¶ 689; Cuyahoga Complaint, ¶ 639.

425 A 25 percent buffer was "added to the APQ annually in 2013 through 2016 to guard against shortages" ("DEA Reduces Amount Of Opioid Controlled Substances To Be Manufactured In 2017," DEA, October 4, 2016, https://www.dea.gov/press-releases/2016/10/04/dea-reduces-amount-opioid-controlled-substances-be-manufactured-2017). Even if one reduced the 2014 quotas by 25 percent, there is still a 14 percent increase in the consolidated quota over the time period 2010-2014 (see backup materials).

426 The decrease into Cuyahoga County was [redacted] percent (Exhibit VI-1).

427 For Cuyahoga County, the position varied from the 37th to 48th percentile for oxycodone and hydrocodone, and from the 39th to 46th percentile for all opioids.

428 Summit Complaint, ¶ 689; Cuyahoga Complaint, ¶ 639.

prescriptions for opioids, yielded orders of unusual size, frequency, or deviation, or raised other warning signs that should have alerted Defendants not only to an overall oversupply in Summit County, but specific instances of diversion."[429] Similarly, in one of their interrogatory responses, Plaintiffs listed over 40 pharmacies in the Counties as "having placed suspicious orders during the relevant time frame."[430]

182. Identifying abnormal orders at the pharmacy level can be expected to require information on the total volume of orders made by the pharmacy at issue, other comparable pharmacies, and the magnitude of usual variations. Likewise, the total volume of orders into a county is a product of the pharmacy-level orders, which are subject to variation based on numerous factors. Of course, an individual Distributor lacking pharmacy operations only would have had information about its own orders from the pharmacy at issue and all other pharmacies in the county, and no information about the orders to other distributors and manufacturers.[431] As a result, any assessment of appropriate variability with respect to the orders received by an individual Distributor would need to account for the unknown presence or absence of orders to other distributors.

183. In contrast, both the DEA and the Ohio BOP have (and had) superior information on the relevant dimensions. The DEA, through CSOS and the ARCOS database, has access to virtually real-time data on shipments by all distributors to pharmacies in a given jurisdiction. Additionally, the Ohio BOP, through the OARRS database, likewise has comprehensive and detailed information on prescribing and dispensing by doctors and pharmacies throughout Ohio as well as

---

429 Summit Complaint, ¶ 705; Cuyahoga Complaint, ¶ 640.

430 The County of Summit, Ohio et al. v. Purdue Pharma L.P. et al., In the United States District Court for the Northern District of Ohio, Eastern Division, Case No. 18-op-45090, Summit County and City of Akron, Ohio Plaintiff's Supplemental Responses and Objections to Distributor Defendants' Interrogatory Number 3 as Rewritten by Special Master David Cohen, December 21, 2018 ("Interrogatory Number 3 Response"), pp. 8-9.

431 A Distributor with pharmacy operations would be aware of the orders by its pharmacy affiliates from other distributors, but not orders by unaffiliated pharmacies from other distributors.

shipments made by distributors to pharmacies.[432] Therefore, the DEA and Ohio BOP have (and had) timely information on: (i) the total shipments of all opioids made to each pharmacy; (ii) the total shipments of all opioids into a given county; and (iii) the information described in (i) and (ii) over time (e.g., daily, monthly, etc.). No private entity has information with this level of accuracy and in such a timely manner.

184. Thus, it is apparent that both the DEA and the Ohio BOP had the requisite information to determine, on a much more accurate and precise basis, the abnormal nature of any order, as compared to any individual Distributor. Further, as discussed earlier in this report, both the DEA and the Ohio BOP (in conjunction with the Ohio SMB) had the regulatory ability and authority to eliminate diversion in a sustained manner. In contrast, I understand that all that an individual Distributor could do would be to refuse the order and report the order to the DEA. That individual Distributor's decision, however, would not be binding on any other Distributor to whom the pharmacy may turn for order fulfillment. As a result, such other Distributor would evaluate whether the order was abnormal using a different set of information, which may or may not result in a different conclusion regarding whether the order was abnormal.

(b) Abnormal Dispensing Volumes

185. Plaintiffs make several references to allegedly abnormal dispensing volumes at both the county and pharmacy levels. For example, at the county level, Plaintiff Summit alleges:

> The Summit County 2010 dose per capita is, according to OARRS, 71.6. [sic] in 2010 and 72.9 in 2012 compared to the ARCOS number of approximately 53.3 for both years. This information,

---

[432] See, for example, Paulozzi, Leonard J. et al., "Controlled Substance Prescribing Patterns—Prescription Behavior Surveillance System, Eight States, 2013," *Morbidity and Mortality Weekly Report: Surveillance Summaries*, 64:9, 2015 ("Paulozzi et al. 2015"), p. 3; "Instructions for Reporting Wholesale Transactions, Suspicious Orders and Customers to OARRS," Ohio BOP, https://www.ohiopmp.gov/Documents/General/WHOLESALE_DISTRIBUTORS/Instructions%20for%20Reporting%20Wholesale%20Transactions,%20Suspicious%20Orders%20and%20Customers%20to%20OARRS.pdf, pp. 2-3.

> along with the information known only to Defendants, would have alerted them to potentially suspicious orders of opioids in and affecting Summit County.[433]

186. On its face, this allegation is nonsensical. As discussed earlier, real-time analysis of ARCOS and OARRS data is not available to Distributors. Further, all a comparison between ARCOS and OARRS would do (and does) is raise questions first about the veracity of both the OARRS and ARCOS data. For example, there are certainly timing differences between shipments into the Counties and prescriptions dispensed within the Counties. In addition, to the extent that ARCOS measures shipments into the Counties and OARRS measures prescriptions dispensed to residents of the Counties, there is no accounting for residents of the Counties filling prescriptions outside the Counties.

187. As a result, Plaintiffs' allegation does not suggest that there were "potentially suspicious orders of opioids" shipped into the Counties. Rather, Plaintiffs' allegation suggests that the DEA and Ohio BOP should have considered the implications of such discrepancies between the ARCOS and OARRS data. It is not apparent that there was anything that an individual Distributor could do, even if it were made aware of the discrepancy on a timely basis.

(c) Abnormal Prescribing Volumes

188. Plaintiffs make several references to abnormally large prescribing volumes at both the county and prescriber levels. At the county level, Plaintiffs allege: "a number of Ohio counties had an opioid prescription rate exceeding their population, and at times well in excess of their population, for extended periods of time [and that,] given this … Defendants should have been on notice that the diversion of opioids was likely occurring in and around Summit County."[434] At the prescriber level, Plaintiffs allege that the pharmacy Defendants, but presumably also Distributors, "failed to adequately use data available to them to identify doctors who were writing suspicious numbers of prescriptions and/or prescriptions of suspicious

433 Summit Complaint, ¶¶ 700- 701. See also Cuyahoga Complaint, ¶ 713.

434 Summit Complaint, ¶¶ 687-688. See also Cuyahoga Complaint, ¶¶ 637-638.

amounts of opioids."[435] More specifically, Plaintiffs bring up several examples of health-care employees, including HCPs, "convicted of crimes involving drug diversion."[436]

189. At the county level, it is apparent from Exhibit VI-2 that Summit County received opioid shipments per capita that varied between the [redacted] to [redacted] percentiles of all counties in the U.S. during the period at issue. Thus, to the extent that "a number of Ohio counties had an opioid prescription rate exceeding their population",[437] it is apparent that one could not infer that Summit County was the source of any diversion to those other counties. Further, to the extent that Plaintiffs allege that Summit County is the source of diversion to other counties, it is not apparent how such an allegation relates to Plaintiffs' claim of damages.

190. At the HCP level, as discussed earlier in this report, an individual pharmacy or even an affiliated chain of pharmacies would have information only about the prescriptions that they dispense. They would not have information regarding the prescribing habits of HCPs. At most, an individual pharmacy could use OARRS to assess the extent to which the pharmacy's patient also had an opioids prescription filled in the last 12 months at any other Ohio pharmacy. In fact, in 2017, approximately 89 million queries of OARRS were made regarding opioid prescriptions for patients, including both HCPs and pharmacists.[438] I understand that an individual pharmacy, however, was not permitted to query the prescribing behavior of HCPs to the extent that behavior was manifest in prescriptions to patients who only used other pharmacies to fill those prescriptions.

---

435 Summit Complaint, ¶ 622. This specific citation refers to the National Retail Pharmacy defendants only; however, Plaintiffs also claim that distributors have access to prescription data and thus were in a position to identify this source of diversion as well (see e.g., Summit Complaint, ¶ 556). See also Cuyahoga Complaint, ¶ 584.

436 Summit Complaint, ¶ 705. See also Cuyahoga Complaint, ¶ 640.

437 Summit Complaint, ¶ 687. See also Cuyahoga Complaint, ¶ 637.

438 "2017 Annual Report Executive Summary," OARRS, https://www.ohiopmp.gov/documents/Annual%20Report%20(2017)%20-%20Executive%20Summary.pdf.

191. In contrast, and as discussed earlier in this report, it is the state PDMPs (OARRS in the case of Ohio) that have the relevant information to address Plaintiffs' allegations. The PDMP is the only entity that, through data submitted by pharmacies, has access to virtually real-time prescribing volumes by all HCPs and dispensing volumes by all pharmacies within a given jurisdiction.[439] Therefore, the Ohio BOP, through the OARRS data, has the timely information on: (i) the total prescribing volumes of all opioids by an HCP; (ii) the total prescribing volumes of all opioids in a given region; and (iii) the information described in (i) and (ii) over time (i.e., daily, monthly, etc.) in order to address Plaintiffs' allegations.

C. Variation in Pharmacy Ordering

192. Most distributors do not observe which patients are dispensed the products that they ship; no distributor is aware of the extent to which patients then divert the opioids dispensed. Nonetheless, I understand that distributors are required to "design and operate a system to disclose to the registrant suspicious orders of controlled substances. Suspicious orders include orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency."[440] In practice, the signals received by the Distributors based on order size are predominantly determined by legitimate prescriptions dispensed by the same pharmacy.

(a) Changes in the Payor Environment

193. Several developments in the payor environment have affected the ordering environment faced by the Distributors. These developments would have complicated the identification of "orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency".[441]

---

439 See, for example, Paulozzi et al. 2015, p. 3.

440 21 CFR 1301.74 (b) (1971).

441 21 CFR 1301.74 (c) (1971).

194. Significant changes to the health care system took place during the period at issue, including the introduction of Medicare Part D in 2006 and the implementation of the Affordable Care Act ("ACA") in 2010.[442] Medicare Part D made prescription drugs, including opioids, more affordable for millions of Americans enrolled in Medicare. Under the ACA, states were granted the option to expand their Medicaid program's coverage in exchange for additional funding from the Federal government,[443] increasing potential access to prescription opioids. Ohio expanded its Medicaid program in 2014.[444]

195. The introduction of Medicare Part D has been associated with increased prescribing of opioids.[445] Between 2007 and 2012, the percentage of Medicare enrollees who received schedule II opioid prescriptions (and who neither had a cancer diagnosis nor were receiving palliative care) for longer than 90 days increased from 1.4 to 2.2 percent, a 57 percent increase.[446]

196. Policies adopted by TPPs also could have an effect on HCP behaviors and outcomes with respect to the prescribing of opioids.[447] One study presents an overview of the coverage and use of utilization management strategies for specific opioid products for low back pain, by insurer type and plan. The authors examine coverage across 50 plans (including Medicaid, Medicare Advantage, and commercial insurance) and find that TPPs did not systematically implement

---

442 Sommers, Benjamin D. et al., "Three-Year Impacts of the Affordable Care Act: Improved Medical Care and Health Among Low-Income Adults," *Health Affairs*, 36:6, 2017; DeLeire, Thomas et al., "Wisconsin Experience Indicates that Expanding Public Insurance To Low-Income Childless Adults Has Health Care Impacts," *Health Affairs*, 32:6, 2013.

443 Jost, Timothy S. and Sara Rosenbaum, "The Supreme Court and the Future of Medicaid," *The New England Journal of Medicine*, 367:11, 2012, p. 983.

444 Gabriel, Trip, "Medicaid Expansion Is Set for Ohioans," *The New York Times*, October 23, 2013.

445 See, for example, Powell, David, et al., "How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D," No. 21072, National Bureau of Economic Research, 2015.

446 Kuo, Yong-Fang et al., "Trends in Opioid Prescriptions Among Part D Medicare Recipients From 2007 to 2012," *The American Journal of Medicine*, 129:2, 2016, p. 221.

447 Waljee, Jennifer F. and Chad M. Brummet, "Opioid Prescribing for Low Back Pain, What Is the Role of Payers?," *JAMA Network Open*, 1:2, 2018, ("Waljee et al. 2018"), pp. 1-2. See also Johnson, Steven Ross, "Insurance plans' opioid policies 'not well-developed to limit their overuse'," *Modern Healthcare*, June 22, 2018, https://www.modernhealthcare.com/article/20180622/NEWS/180629964.

policies to discourage the use of opioids or to limit their utilization.[448] There was limited use of step therapy;[449] when such policies were used, the requirements often failed to integrate any non-pharmacologic therapies.[450] Of the 15 state Medicaid plans examined, 42 percent required prior authorization for covered opioids, 69 percent used quantity limits, and 9 percent used step therapy. Among Medicare Advantage plans, "most commonly used quantity limits for extended-release/long-acting opioids and never used step therapy for opioids."[451] Quantity limits were generally observed for a 30-day supply but not necessarily for a shorter supply.[452]

197. Another study examined Medicare formulary coverage restrictions of prescription opioids over time, using data from over 200 formularies each in 2006, 2011, and 2015. In 2006 and 2011, over two thirds of drug-dosage opioid combinations were free from any coverage restrictions; by 2015, this had decreased to a third. Throughout the years examined, a negligible number of formularies required step therapy, but prior authorization requirements increased modestly to 4.4 percent of plans in 2015. Quantity limits were the most commonly utilized form of restriction to opioid coverage, with the median proportion of drug-dosage combinations with quantity limits increasing from 8.9 percent in 2006 to 71.1 percent in 2015.[453]

---

448 Lin, Dora H. et al., "Prescription Drug Coverage for Treatment of Low Back Pain Among US Medicaid, Medicare Advantage, and Commercial Insurers," *JAMA Network Open*, 1:2, 2018, ("Lin et al. 2018"), pp. 2, 8-10.

449 Step therapy or "fail first" "is a process used by health insurers to control costs. It requires patients to try one or more medications specified by the insurance company, typically a generic or lower cost medicine, to treat a health condition. Patients must then fail on the medication(s) before allowing a "step up" to another medicine that may be more expensive for the insurer." ("Step Therapy," Prescription Process, http://prescriptionprocess.com/barriers-to-access/step-therapy/).

450 Lin et al. 2018, p. 8.

451 Lin et al. 2018, Table 3, p. 8.

452 Lin et al. 2018, p. 10.

453 Samuels, Elizabeth A. et al., "Medicare Formulary Coverage Restrictions for Prescription Opioids, 2006 to 2015," *Annals of Internal Medicine*, 167:12, 2017, ("Samuels et al. 2017"), p. 895.

198. TPP formulary design may influence the decision to prescribe an opioid with or without an ADF. Opioids with ADFs are generally more expensive than their non-abuse deterrent counterparts; accordingly, TPPs have a financial incentive to favor non-ADF opioids.[454] One review of public and private health insurance formularies revealed that controlled-release oxycodone was, in some cases, restricted or excluded from Medicare formularies.[455] Another study found that TPPs were "reluctant to pay for the more expensive OxyContin even prior to its reformulation for enhanced safety," instead opting for cheaper alternatives such as hydrocodone, "resulting in increased use and abuse of less expensive and more dangerous opioids".[456] According to another study, after the reformulation of OxyContin, low reimbursement of ADFs remained a key barrier to uptake.[457] In general, TPPs were reluctant to update their coverage to reflect changes in prescribing guidelines.[458]

199. Lately, TPPs have begun taking more aggressive measures in limiting opioid utilization. In a survey of state Medicaid programs, 34 states disclosed adoption or planned adoption of the CDC Guidelines in their fee-for-service programs during fiscal year 2018.[459] State Medicaid uptake of the CDC Guidelines may, in part, be driven by the "opportunity to receive federal financial participation (FFP)

---

454 "Abuse-Deterrent Formulations of Opioids: Effectiveness and Value," Institute for Clinical and Economic Review, August 8, 2017, p. ES6.

455 Argoff, Charles E. et al., "Validity testing of patient objections to acceptance of tamper-resistant opioid formulations," *Journal of Pain Research*, 2013:6, 2013, p. 369.

456 Schatman, Michael E. and Lynn R. Webster, "The health insurance industry: perpetuating the opioid crisis through policies of cost-containment and profitability," *Journal of Pain Research*, 2015:8, 2015, p. 155; Cicero, Theodore J. et al., "Multiple Determinants of Specific Modes of Prescription Opioid Diversion," *Journal of Drug Issues*, 41:2, 2011, p. 9.

457 Huskamp, Haiden A. et al., "Coverage of Medications That Treat Opioid Use Disorder and Opioids for Pain Management in Marketplace Plans, 2017," *Medical Care*, 56:6, 2018, ("Huskamp et al. 2018"), p. 506, Table 2.

458 Lin et al. 2018, p. 10.

459 Gifford, Kathleen et al., "Medicaid moving ahead in uncertain times: Results from a 50-State Medicaid Budget Survey for State Fiscal Years 2017 and 2018," Kaiser Family Foundation, October 2017, ("Gifford, et al., 2017"), pp. 4, 64. I understand that Ohio Medicaid has not officially adopted the CDC Guidelines. Dr. Mary Applegate, Medical Director of Ohio Medicaid, has testified that Ohio Medicaid follows Ohio's state guidelines, which are described as stricter than the CDC Guidelines (Deposition of Mary Applegate, M.D., March 28, 2019, p. 279).

for the continuum of services to treat addiction to opioids or other substances."[460] One of the requirements to receive FFP is for states to "demonstrate how they are implementing evidence-based treatment guidelines" alongside broader initiatives to inhibit opioid abuse.[461]

200. Additionally, it is apparent that private insurers are increasingly aligning their opioid management programs to the CDC Guidelines.[462] For example, in 2016, Anthem Blue Cross and Blue Shield in Ohio limited coverage of opioids to seven days for those newly starting a prescription for opioids and began requiring prior authorizations for all long-acting opioids. Anthem Blue Cross and Blue Shield also began restricting patients it had identified as being the most at-risk for developing an opioid use disorder to use only one pharmacy and/or provider for their opioid prescriptions.[463]

201. In April 2018, the Centers for Medicare & Medicaid Services ("CMS") published new limits for high-dose opioid prescriptions for Medicare Part D users.[464] The limits are planned for implementation in 2019 and are aligned with the CDC Guidelines. A summary of the policy highlights that:

> High dosage thresholds are outlined [including] parameters for prescriptions greater than 90 MME, which state a pharmacist should consult with [a] prescriber and document the discussion. At 200 MME, a hard cap is implemented that can only be overridden by the plan sponsor. Additional guidelines for opioid naïve

460 Letter from Brian Neale, State Medicaid Director, Subject: Strategies to Address the Opioid Epidemic, November 1, 2017, https://www.medicaid.gov/federal-policy-guidance/downloads/smd17003.pdf, ("Letter from State Medicaid Director, 2017"), p. 2.

461 Letter from State Medicaid Director, 2017, p. 3.

462 See, e.g., "New opioid management program for Commercial, Medicaid, and Exchange plans," Fallon Health, https://www.fchp.org/providers/pharmacy/opioid-management.aspx.

463 "Anthem Blue Cross and Blue Shield helps to reduce opioid use in Ohio by 16 percent among its members," Anthem Press Release, August 23, 2017, https://www.anthem.com/press/ohio/anthem-blue-cross-and-blue-shield-helps-to-reduce-opioid-use-in-ohio-by-16-percent-among-its-members/.

464 "2019 Medicare Advantage and Part D Rate Announcement and Call Letter," CMS Press Release, April 2, 2018, https://www.cms.gov/newsroom/fact-sheets/2019-medicare-advantage-and-part-d-rate-announcement-and-call-letter.

patients were also included, limiting initial opioid prescriptions to no more than a 7 days' supply for the treatment of acute pain.[465]

(b) Other Relevant Changes in the Demand Environment

202. Additional developments in the demand environment have likewise affected the ordering environment faced by the Distributors. These developments would have complicated the identification of "orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency."[466]

203. In December 2013, as a result of a vote held by the FDA's Public Advisory Committee, the FDA recommended to the DEA that hydrocodone-combination products such as Lortab and Vicodin be rescheduled from schedule III to schedule II. On February 27, 2014, the DEA announced its intention to reschedule hydrocodone-combination products and solicited public input on its proposed policy change. The DEA claimed that the purpose of this "up-scheduling" was because of the "substantial evidence of high potential for abuse of [hydrocodone-combination products]."[467] On August 22, 2014, the DEA formally announced its intention to reclassify hydrocodone-combination products and announced the policy would take effect in 45 days, on October 6, 2014.[468]

204. Moving a drug from schedule III to schedule II has implications regarding the dispensing and distribution of that product. There is an increased regulatory burden associated with schedule II products as compared to schedule III products. For example, as discussed earlier in this report, there are more onerous storage requirements associated with schedule II products.[469] Additionally, in ordinary

---

465 "CMS Announces New Guidelines on High-Dose Opioids," Affirm Health, https://www.affirmhealth.com/blog/medicare-announces-new-guidelines-on-high-dose-opioids.

466 21 CFR 1301.74 (c) (1971).

467 21 CFR Part 1308 (2014).

468 21 CFR Part 1308 (2014).

469 See, for example, Yeh, Brian T., "The Controlled Substances Act: Regulatory Requirements," *Congressional research Service*, 2012 ("Yeh 2012"), p. 12; "Electronic Code of Federal Regulations," *Electronic Code of Federal Regulations*, https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=3903114e1ff47360902eec29a1f38046&ty=HTML&h=L&r=PART&n=pt21.9.1301; Sullivan, Thomas, "DEA Places Heavy Restrictions on Vicodin and Other

cases, pharmacies (and other dispensers) can only dispense prescriptions for schedule II products if the prescription is presented in written form and signed by the prescriber; schedule II prescriptions cannot be refilled. In contrast, prescriptions for schedule III-V products may be written, orally communicated, or faxed to a pharmacy, and can be refilled up to five times in a 6-month period.[470]

205. Potentially as a result of the differences highlighted above, [redacted]

206. Other changes to the demand environment that would affect the ability of individual Distributors to accurately and precisely identify diversion include the following.

(a) Several new prescription opioid products have been launched since 2006, including a reformulated OxyContin, Onsolis (fentanyl), and Embeda (morphine).[471] Shipments for these products would be highly variable as demand is established and pharmacies stock the product. For example, the launch of the ADF reformulation of OxyContin in 2010 would be expected to lead to a surge in shipments as pharmacies stock the product in advance of demand.[472]

(b) As discussed earlier in this report, a number of organizations issued new or revised prescribing guidelines for opioids since 2006: the VA/DOD

Hydrocodone Combination Drugs; Gives Stakeholders 45 Days to Adjust," *Policy and Medicine*, 2018, https://www.policymed.com/2014/09/deaheavyrestrictionsonvicodin.html.

470 Gabay, Michael, "The Federal Controlled Substances Act: Controlled Substances Prescriptions," *Hospital Pharmacy*, 48:8, 2013.

471 "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," FDA, February 2019, https://www fda.gov/media/106638/download.

472 "FDA Approved Drug Products," Drugs@FDA, NDA 022272, https://www.accessdata fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022272.

Guidelines in 2010 and 2017;[473] the CDC Guidelines in 2016;[474] the AAFP Guidelines in 2016;[475] and the Ohio Guidelines in 2018.[476] It is expected that shipments would be more variable as these guidelines begin to influence prescribing behavior.[477]

(c) Variation Across and Within Pharmacies

207. Analyses of ARCOS data, along with other data produced by Distributors, indicates a high degree of variation in pharmacy orders, taking place along several dimensions. These include: variation in ordering from one pharmacy to another; variation in ordering within each pharmacy during the course of a year; and variation in ordering within pharmacies over time. Each source of variation would have complicated the identification of "orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency."[478]

208. With respect to opioid orders across pharmacies, Exhibits VI-4 and VI-5 show average monthly oxycodone and hydrocodone orders by pharmacies in the Counties in 2012, conditional on placing at least one order for either of these molecules. There is significant variation among the pharmacies. In Cuyahoga County, the median pharmacy has an average monthly order of 6,897 dosage units and the interquartile range is 282 to 14,720 dosage units. In Summit County, the median pharmacy has an average monthly order of 10,148 dosage units and the interquartile range is 658 to 21,340 dosage units.

---

473 VA/DoD 2010, pp. 3-73; VA/DoD 2017, pp. 3-198.

474 Dowell et al. 2016, pp. 1624-1645.

475 Lembke et al. 2016, pp. 982-990.

476 Ohio State Medical Board 2018.

477 See, for example, Howard, Ryan et al., "Reduction in Opioid Prescribing Through Evidence-Based Prescribing Guidelines," *JAMA Surgery*, 153:3, 2018 ("Howard et al. 2018"), pp. 285-287; Franklin, Gary M. et al., "Bending the Prescription Opioid Dosing and Mortality Curves: Impact of the Washington State Opioid Dosing Guideline," *American Journal of Industrial Medicine*, 55, 2012 ("Franklin et al. 2012), p. 326.

478 21 CFR 1301.74 (c) (1971).

209. Variation in opioid ordering does appear to be a function of a pharmacy's overall "size". For example, the correlation between McKesson's shipments of opioids and non-controlled products into the same pharmacies in 2012 is 0.74 for Cuyahoga County and 0.86 for Summit County; the correlation for Cardinal is 0.41 for the Counties together. All of these correlations are significant at the 95 percent level. Thus, pharmacies with lower order volumes of other products tend have lower order volumes for opioids.

210. Nonetheless, within a given pharmacy, monthly orders vary to a considerable degree over the course of a year. Exhibits VI-6 and VI-7 show monthly orders of oxycodone and hydrocodone for pharmacies in Cuyahoga and Summit Counties, respectively, in 2012 (selecting pharmacies with ordering between the 50th and 75th percentiles). Each point on the x-axis (i.e., each "column" of dots) corresponds to a different pharmacy, and the dots correspond to the orders in each of the 12 months during the year.

211. Orders also vary considerably over longer periods of time within pharmacies. Exhibits VI-8 and VI-9 show annual orders of oxycodone and hydrocodone for all pharmacies in the Counties in each of 2006 and 2012. Each column again represents a separate pharmacy, with an arrow representing that pharmacy's change in orders between 2006 (the beginning of the arrow) and 2012 (the end of the arrow). The sample is restricted to pharmacies whose total ordering (for the years 2006 and 2012) falls between the 25th and 75th percentiles. It is evident that within an average pharmacy, ordering increased over this period; for example, in Cuyahoga County, the median increase in oxycodone and hydrocodone orders from 2006 to 2012 was 49 percent.[479] Note that over the same period, the DEA's national quota for oxycodone increased by 71 percent, with the quota for hydrocodone increasing by 87 percent.

212. Accordingly, there is significant variation in the ordering behavior among different pharmacies, as well as significant variation within the ordering patterns

[479] The median increase for pharmacies in Summit County was 33 percent.

of individual pharmacies over time. These results demonstrate the difficulty and imprecision that confronts each individual Distributor. A Distributor only was able to use its own ordering pattern from different pharmacies at the same time and the same pharmacy over time to determine suspicious orders as compared to legitimate orders.[480] Further, legitimate order sizes may vary due to legitimate changes in demand that were the result of standard variability, the introduction of Medicare Part D and the ACA, the change in schedule for hydrocodone-combination products, and the introduction of new products and guidelines for opioid prescribing. Two pharmacies that otherwise appear similar could have legitimate yet very different ordering patterns, just as one pharmacy's legitimate ordering pattern could change over time.

(d) Variation in Prescribing

213. Pharmacy orders are driven by prescribing behavior. Variations in legitimate prescribing behavior could generate variations in pharmacy orders that, if shipped, would be inappropriate to flag as Distributor misconduct.

214. First, opioid prescribing varies significantly across HCPs within the Counties. Using IQVIA data, Exhibits VI-10 and VI-11 show the average monthly prescribing of oxycodone and hydrocodone among HCPs in the Counties for 2012. Focusing on the interquartile range, prescribing of oxycodone and hydrocodone ranged from 46 to 524 dosage units in Cuyahoga County and from 52 to 746 dosage units in Summit County. Determining whether any of the individual prescriber behavior was inappropriate would require analysis at the HCP / patient level and substitution for the medical judgment of an HCP in good standing with the Ohio SMB as it relates to the prescribing of opioids.

215. Second, opioid prescribing varies considerably even for the same HCPs. Exhibits VI-12 and VI-13 present monthly prescriptions of oxycodone and hydrocodone for 100 randomly chosen HCPs between the 25th and 75th percentiles (in terms of total dosage units in 2012) in Cuyahoga and Summit Counties,

480 Again, an exception is those Distributors with pharmacy operations, which observe orders by affiliated pharmacies from other distributors.

respectively. Each point on the x-axis corresponds to a different HCP and the markers correspond to the total number of prescriptions in each month during 2012. Based on the prescribers included in the figure, the median difference between the smallest (non-zero) and largest monthly number of oxycodone or hydrocodone prescriptions was 571 and 543 percent in Cuyahoga and Summit Counties, respectively.

216. Third, there are additions and subtractions to prescribers in the Counties over time. Exhibits VI-14 and VI-15 show the number of "new" opioid prescribers appearing in each County and the number of HCPs who "leave" each County.[481] Using Cuyahoga County as an example, there are an average of 26 new prescribers and 21 leaving prescribers each month, as compared to 3,738 prescribers that persist from one month to the next. January 2004 had the largest net increase, 69 prescribers, while November 2016 had the largest net decrease, 52 prescribers. The prescribing behavior of those who enter and leave the group of HCPs prescribing opioids each month adds more variability to pharmacy orders.

217. Fourth, based on data from OARRS, most pharmacies fill prescriptions written by a significant number of prescribers. Exhibit VI-16 shows the distribution of the total number of prescribers per pharmacy in the Counties during 2012. Pharmacies fill prescriptions written by up to 2,126 HCPs, with a median of 272. An implication of this is that orders from most pharmacies aggregate prescribing by multiple practitioners, none of whom is particularly dominant. Given the prescribing and ordering variability noted above, a Distributor is unlikely to be able to identify diversion due to a particular prescriber.

218. In summary, prescribing underpins the ordering of prescription opioids by pharmacies and adds a further degree of complexity to the identification of diversion by Distributors. Individual Distributors would have understood that a

[481] If an HCP appears in any year from 1999 or later with no history, they are defined as "new". Similarly, if an HCP is no longer observed prescribing starting at some point in 2016 or earlier, they are defined as having "left".

considerable amount of the variation in their orders could be driven by this variation in prescribing. Further, to the extent that this variation in prescribing is driven by legitimate medical needs, the variation in pharmacy ordering reflects those legitimate medical needs.

D. Inferring the Prevalence of Diversion at the County Level

219. I understand that Plaintiffs claim Distributors failed to prevent an excessive quantity of prescription opioid doses from entering circulation in the Counties.[482] As discussed above, however, the regulatory obligations of individual Distributors under the CSA do not (and cannot) extend to the monitoring of the total volume of prescription opioids into a particular geography. Individual Distributors have only their own data for consideration; unlike the DEA, individual Distributors do not have real-time information on the shipments of all distributors and manufacturers into the Counties. Nonetheless, I ask whether any data exist that support the contention that shipments into the Counties were excessive relative to expected medical requirements, on the basis of: (i) potentially identifiable sources of diversion such as "doctor shopping" or "pharmacy shopping" or HCPs charged with illegally distributing controlled substances; and (ii) expected total shipments based on local medical conditions and prescribing guidelines. I find that there is little basis to expect that activities associated with diversion would account for a large volume of opioid prescriptions, making it more difficult to detect diversion.[483]

(a) Doctor Shopping and Pharmacy Shopping

220. The practice of "doctor shopping" is characterized by patients "obtaining controlled substances from multiple healthcare practitioners without the prescribers' knowledge of the other prescriptions."[484] The related practice of

---

482 See, for example, Summit Complaint, ¶ 689; Cuyahoga Complaint, ¶ 639.

483 The Keyes Report also notes that "doctor shopping" was rare and that PMCs "do not explain in any significant way the expansion of opioid prescribing and opioid-related harms in the U.S." (Keyes Report, p. 18).

484 "Doctor Shopping Laws," Public Health Law, CDC, https://www.cdc.gov/phlp/docs/menu-shoppinglaws.pdf.

"pharmacy shopping" involves patients obtaining controlled substances from multiple pharmacies. Doctor and pharmacy shopping represent forms of diversion that have received attention in the literature.[485] The potential for doctor or pharmacy shopping was one of the rationales for implementing PDMPs, as noted above.

221. The prevalence of doctor shopping is one indicator of the potential volume of prescription opioids that are suspected of diversion. In Ohio, however, doctor shopping appears to be rare. A study performed by OARRS estimates that only 0.03 to 0.09 percent of patients prescribed opioids in Ohio from 2009 through 2015 may be suspected of doctor shopping under the definition employed by OARRS for the analysis.[486]

222. I also analyze data provided by OARRS to assess the extent of doctor shopping in the Counties. For the purposes of my analysis, I consider a "doctor shopper" to be an individual receiving an opioid prescription from ten or more HCPs in a calendar year. This definition differs from that used by OARRS, which defines doctor shopping as filling an opioid prescription at five or more pharmacies written by five or more HCPs in a calendar month.[487] As shown in Exhibit VI-17, between 2008 and 2017, only 0.1 to 0.3 percent of patients filled opioid prescriptions in the Counties written by ten or more HCPs in a calendar year; these patients accounted for only 0.4 to 1.8 percent of dosage units dispensed in those years. Note that this behavior would only be visible to Distributors to the extent that the patients at issue filled the different prescriptions at the same pharmacy (including chain affiliates) and that pharmacy or chain is a Distributor.

223. I have also performed a similar analysis to assess the extent of pharmacy shopping; these results are shown in Exhibit VI-18. For the purposes of my

485 See, for example, Paulozzi et al. 2015, pp. 1-3; Yang, Zhuo et al., "Defining risk of prescription opioid overdose: pharmacy shopping and overlapping prescriptions among long-term opioid users in Medicaid," *The Journal of Pain*, 16:5, 2015, pp. 445-453.

486 "State Statistics," OARRS, https://www.ohiopmp.gov/State.aspx.

487 "State Statistics," OARRS, https://www.ohiopmp.gov/State.aspx.

analysis, I consider a "pharmacy shopper" to be an individual filling an opioid prescription at ten or more pharmacies in a calendar year. Between 2008 and 2017, 0.01 to 0.1 percent of patients filled opioid prescriptions at ten or more pharmacies in a calendar year; these patients accounted for only 0.05 to 1.3 percent of dosage units dispensed in the Counties at issue during those months. These levels would not appear to be indicative of illegal diversion operating on a scale that could be detected on the basis of orders of unusual size, pattern, or frequency.

(b) Illicit Prescriber and Pharmacy Behavior

224. Another potential form of diversion involves "rogue prescribing" by individuals responsible for prescribing a disproportionate number of opioids.[488] The number of opioids prescribed is visible to state BOPs via PDMPs. Accordingly, if rogue prescribing represented a significant source of diversion of prescription opioids, one would expect to see law enforcement actions and/or disciplinary proceedings involving prescribers that account for a significant share of opioid prescribing in a given geography.

225. I have been provided with a list of HCPs who operated in Cuyahoga or Summit County and whose licenses were put on probationary status, suspended, surrendered, or revoked in connection with misconduct involving opioids.[489] As shown in Exhibits VI-19 and VI-20, according to IQVIA data, during the period 1997 to 2017, these prescribers accounted for at most 10 percent of opioid prescribing in Cuyahoga County, and 4 percent in Summit County. These amounts are driven by a small number of individual HCPs. For example, in Cuyahoga County in 2011 (the year that this share of prescribing peaked), four prescribers accounted for 88 percent of the prescribing volume of those HCPs charged with illicit dealing; in Summit County in 2011, one prescriber accounted

[488] Plaintiffs note several examples of HCPs "convicted of crimes involving drug diversion" (see, for example, Summit Complaint, ¶¶ 705-708; Cuyahoga Complaint, ¶¶ 640-643).

[489] Appendix B.

for 97 percent of the prescribing volume of those HCPs charged with illicit dealing.[490]

226. I also am provided with a list of pharmacies whose licenses were suspended or revoked in connection with misconduct involving opioids in the Counties.[491] Only one such pharmacy was identified in 1999 and none since 2000; accordingly, this pharmacy's orders do not appear in the ARCOS data.

227. In both cases, these trends would not appear to be indicative of illegal diversion that operated on a scale that would be readily apparent to Distributors on the basis of orders of unusual size, pattern, or frequency.

(c) Expected Total Shipments

228. Next, I consider whether shipments into the Counties may have been appropriate given information on the prevalence of various conditions coupled with prescribing guidelines. I focus on a condition for which prescription opioids were known to be used during the period at issue: the treatment of chronic pain for arthritis.[492] I construct an estimate of total potential prescription opioid utilization in each of the Counties in 2010, based on information regarding population, incidence, and expected dosing.

229. This analysis generates results that are presented in Exhibits VI-21 and VI-22. Potential opioid utilization for this condition is estimated to be 800 million MME for Cuyahoga County and 331 million MME for Summit County. These amounts exceed by a significant amount the actual shipments made by any given Distributor in 2010; for example, according to ARCOS, McKesson shipped 123 million MME into Cuyahoga County and 106 million MME into Summit County, respectively. At most, any Distributor's ARCOS shipments accounted

490 See backup materials. Note that it is not apparent to me how much of the prescribing volume of those charged with illicit dealing was inappropriate.

491 Appendix B.

492 I note that prescription opioids were also used for many other conditions, such as end of life treatment for cancer pain; however, I do not attempt to quantify the expected utilization based on these other conditions.

for 27 percent of MME potentially required in Cuyahoga County for the treatment of chronic pain for arthritis and 45 percent of MME potentially required in Summit County. Further, this analysis is conservative as it only considers one of the conditions for which opioids tend to be prescribed.

VII. EFFECTIVENESS OF ACTIONS ON THE SIGNALS OF DIVERSION

230. Plaintiffs make certain claims regarding Distributors' alleged failure "to report suspicious orders, prevent diversion, or otherwise control the supply of opioids."[493] Implicit is the premise that by acting more aggressively to report and/or block orders placed by pharmacies, Distributors could have limited diversion, thereby reducing the burdens of misuse, abuse, and/or addiction, presumably without hurting patients with real medical needs. This premise is flawed.

231. Distributors reported a significant number of "suspicious" orders to the DEA. Electronic records produced by the DEA indicate that at least [redacted] orders nationwide, [redacted] orders in Ohio, and [redacted] orders in the Counties were reported to DEA headquarters as "suspicious" during the period 2006 to 2014. To the extent that this number does not include all reports to DEA headquarters, reports to DEA field offices, or reports that were not submitted electronically, then the figure is understated. An examination of the outcome of orders reported to the DEA as "suspicious" reveals that in the vast majority of instances, the pharmacies that were the subject of the order report continued ordering without any apparent consequences. In fact, I am not aware that the DEA has taken any action against pharmacies in the Counties as a result of the hundreds of reports of "suspicious" orders.[494] Accordingly, it is apparent that Plaintiffs' premise that more aggressive

493 Cuyahoga Complaint, ¶ 547; Summit Complaint, ¶ 579.

494 I note that Thomas Prevonik, Chief of Pharmaceutical Investigations at DEA, testified that even assuming all DEA actions are undertaken in response to "suspicious" order reports, less than 1 percent of "suspicious" order reports resulted in DEA action (Deposition of Thomas Prevoznik, 30(b)(6) Witness on Behalf of the DEA, April 18, 2019 ("Prevoznik Deposition"), pp. 579-583).

"suspicious" order reporting would have led to a significant reduction in prescription opioid shipments is not supported.

A. Number of "Suspicious" Orders Reported

232. Information on "suspicious" order reports ("SORs"), identified by the DEA as being submitted electronically to DEA headquarters during the period 2006 through 2014, is summarized in Exhibit VII-1. The DEA data identify [redacted] SORs for pharmacies based in Ohio and [redacted] SORs for pharmacies based in the Counties.[495] Conditional upon having an order reported to the DEA, the average pharmacy in Ohio had [redacted] SORs and [redacted] unique months with a SOR during the nine-year period; the average pharmacy in the Counties had [redacted] SORs and [redacted] unique months with a SOR.

233. As also shown in Exhibit VII-1, [redacted] pharmacies in the Counties were associated with at least one SOR during the period; in most cases, pharmacies were associated with multiple SORs in any given month. Exhibit VII-1 also shows the number of months that a pharmacy was associated with at least one SOR. Conditional upon having at least one SOR, the average pharmacy was associated with SORs for 4 months. The results are similar for Ohio overall, suggesting that the pharmacies in the Counties did not exhibit unusual behavior with respect to SORs.

234. Plaintiffs contend that these SORs were insufficient, and that as much as 85 percent of the opioid shipments to customers in the Counties were in excess of what was "medically necessary."[496] To the contrary, based on at least the reasons listed below and discussed earlier in this report, Plaintiffs' estimates would block shipments far in excess of what could plausibly be explained by diversion, at the expense of patients with legitimate medical needs.

---

495 These counts exclude buprenorphine or NDC codes that are not included in the ARCOS data.

496 McCann Report, ¶¶ 156-158; Summit Complaint, ¶ 14; Cuyahoga Complaint, ¶ 14.

(a) A study performed by OARRS estimates that only 0.03 to 0.09 percent of patients prescribed opioids in Ohio from 2009 through 2015 may be suspected of doctor shopping.[497]

(b) As noted above, prescribing by physicians subsequently subject to discipline or otherwise suspected of excessive prescribing accounted for no more than 10 percent of dosage units prescribed in Cuyahoga County and no more than 4 percent of dosage units prescribed in Summit County in any given year during the time period at issue.[498]

(c) In statements made to Congress in April 2014, the DEA indicated that 99.5 percent of prescribers are not overprescribing.[499]

235. Accordingly, Plaintiffs would appear to be advancing the position that Distributors should have prevented HCP overprescribing of opioids and should have blocked orders to patients with legitimate medical needs. Yet, Distributors have virtually no information that could be used to second-guess the prescribing decisions of the HCPs who see patients. Further, I am not aware of a requirement that Distributors block orders intended to fill prescriptions that HCPs assessed as appropriate for medical use, nor am I aware that individual Distributors have a regulatory obligation to monitor and/or act on signals of excessive prescribing, let alone have the ability to do so. As discussed earlier in this report, individual Distributors only had information regarding the orders submitted to them and the shipments made by them; only in certain limited circumstances did an individual Distributor have any knowledge of a specific prescription for a specific patient written by a specific HCP, and that knowledge was restricted to the prescriptions dispensed by that individual Distributor through its affiliated pharmacies.

---

497 "State Statistics," OARRS, https://www.ohiopmp.gov/State.aspx.

498 See Appendix B and Exhibits VI-20 and VI-21.

499 "Examining the Growing Problems of Prescription Drug and Heroin Abuse," Hearing before the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, p. 76, https://www.govinfo.gov/content/pkg/CHRG-113hhrg90923/pdf/CHRG-113hhrg90923.pdf. See also Prevoznik Deposition, pp. 436-445, explaining that from 2012, 98 or 99 percent of prescribers did not overprescribe.

Plaintiffs also have not articulated any means by which Distributors could have verified that enhanced reporting and non-shipment of orders would not deprive legitimate patients of medically necessary pain relief. This failure to take into account the costs of more aggressive reporting and non-shipments necessarily leads to Plaintiffs' excessive levels of allegedly improper orders.

B. Activity Subsequent to Reporting of Orders

236. It is relevant to consider what appears to have happened to pharmacy ordering following the submission of SORs. Using the ARCOS data, I test for a relationship between SORs and the likelihood that a pharmacy, at some point, is no longer observed making opioid orders (which I refer to as "exit"). For the purposes of this analysis, I define a pharmacy as exiting if there exists a date prior to July 1, 2014, at which from that point onward (through December 31, 2014), the pharmacy is not observed making any opioid orders. In order to allow for a delay between an SOR and possible consequences, I limit my analysis to those pharmacies for which the last SOR as reported by the DEA was no later than June 1, 2014. I also construct a "control group" of pharmacies that were not associated with any SORs as reported by the DEA.[500]

237. The results of this analysis at the national, Ohio, and County level are summarized in Exhibit VII-2. As shown, the rate at which pharmacies exit is approximately the same in the control group as it is for those pharmacies associated with SORs. Specifically, in the national sample, [redacted] percent of pharmacies associated with SORs place no orders from July 2014 forward; this compares to [redacted] percent of pharmacies in the control group. The difference

[500] The control group was constructed using the following methodology: (i) For each pharmacy, calculate a rolling 6-month average of monthly shipments by MME; (ii) for each pharmacy whose last reported order is no later than June 1, 2014, define the month prior to the month of the first reported order as the "matching month"; (iii) for each pharmacy whose last reported order is no later than June 1, 2014, find all pharmacies in the matching month with no observed reported order (up to December 31, 2014), of the same type (i.e., "retail chain", "independent pharmacy", etc.), and in the same county, and with a rolling 6-month average within 0.2 times and 5 times the rolling 6-month average of the target pharmacy; and (iv) of these pharmacies, choose the one whose rolling 6-month average is closest to that of the reported pharmacy in the month prior to its first reported order. If no match is found then the pharmacy is dropped from the analysis.

suggests a small negative effect of SORs on subsequent orders at the national level. In Ohio and for the Counties, however, the exit rate of pharmacies associated with SORs is less than the exit rate of the control group.

238. There may be a number of reasons that pharmacies exit, but my analysis does not suggest that DEA activity following an SOR led to a higher rate of pharmacy exit in the Counties. As a result, and contrary to Plaintiffs' assertion, it is not apparent that more SORs would have led to a significant reduction in the availability of prescription opioids in the Counties during the period from 2006 through 2014.

VIII. LACK OF SUPPORT FOR CAUSAL LINKS

A. Introduction

239. As I understand the claims advanced by Plaintiffs that relate to Distributors, they can be decomposed into the following constituent parts:

(a) Distributors were positioned to detect excessive prescribing by doctors, and excessive ordering of prescription opioids by pharmacies in the Counties;[501]

(b) More aggressive reporting and/or non-shipment of orders by Distributors would have eliminated the excessive supply of prescription opioids to the Counties and reduced the level and incidence of prescription opioid misuse and abuse, while simultaneously having no negative effects on patients who were using prescription opioids for legitimate medical purposes;[502]

[501] Summit Complaint, ¶ 702a; Cuyahoga Complaint, ¶ 525a.

[502] Summit Complaint, ¶ 702d; Cuyahoga Complaint, ¶ 525d.

(c) By not eliminating the excessive supply, Distributors directly caused the growth in dependence on prescription opioids, leading to the formation of a population of prescription opioid misusers;[503]

(d) Prescription opioid misuse led in many cases to addiction, prescription drug overdoses, and other harms;[504]

(e) The growth in dependence on prescription opioids created a stock of individuals susceptible to illicit opioid use and abuse;[505]

(f) When the availability of prescription opioids declined after 2010, many of these individuals turned to illicit opioids, particularly heroin, resulting in problems of addiction, overdose, and other harms, which have fallen on the Counties;[506]

(g) Mortality accelerated after 2013 as drug traffickers started to incorporate fentanyl as a lower-cost alternative to heroin and the harms associated with fentanyl have fallen on the Counties.[507]

240. Weaknesses in points (a) and (b) have been identified and discussed in the preceding sections of this report.

(a) Individual Distributors possessed information only about their own orders and shipments of opioids. As such, individual Distributors did not have information about the total supply of opioids into the Counties.

(b) Only in certain circumstances did an individual Distributor have any knowledge of a specific prescription for a specific patient written by a specific prescriber and that knowledge was restricted to the prescriptions

503 Summit Complaint, ¶¶ 555, 714; Cuyahoga Complaint, ¶¶524, 645; Gruber Report, ¶ 29.

504 Summit Complaint, ¶¶ 715-745; Cuyahoga Complaint, ¶ 646.

505 Summit Complaint, ¶¶ 6, 1057; Cuyahoga Complaint, ¶¶ 6, 1087; Gruber Report, ¶ 16.

506 Summit Complaint, ¶¶ 316-317; Cuyahoga Complaint, ¶¶ 285-286; Gruber Report, ¶¶ 46, 50-51, 65.

507 Gruber Report, ¶¶ 55, 70.

dispensed by that individual Distributor through its affiliated pharmacies. As such, individual Distributors did not have information about prescriptions dispensed to patients or prescriptions written by HCPs that were not filled at pharmacies that the individual Distributor operated, to the extent that the individual Distributor operated any pharmacies.

(c) In contrast to the isolated and limited information of each individual Distributor, the DEA, Ohio BOP, Ohio SMB, Ohio Medicaid, and Ohio WCB all had access to complete and timely information that could have been used to identify apparent diversion and conduct consequential regulatory and enforcement actions to curtail diversion in a sustained manner.

(d) Despite at least [redacted] SORs reported in the data provided by the DEA, the DEA, Ohio BOP, Ohio SMB, and other regulatory agencies took no action against any pharmacies, and action against only 22 physicians in the Counties.[508]

(e) SORs did not lead to apparent increase in exit activity among pharmacies in the Counties.

(f) Distributors do not have the ability to second-guess the opioid prescribing decisions, presumably made after an appropriate patient consultation, of HCPs in good standing with the DEA and the Ohio SMB.

(g) Plaintiffs do not support credible estimates of the excessive supply of prescription opioids such that increased SORs and/or non-shipment of orders would have led to a decline in diversion and the costs (if any) incurred by the Counties as a result of that diversion without also reducing the ordering and dispensing of prescription opioids for those with legitimate medical needs.

[508] See Exhibit VI-X and Appendix B.

241. In this section, I address other aspects of the causal chain articulated by Plaintiffs.

(a) First, as discussed earlier in the report, substance abuse has been a scourge on the U.S. for decades, long preceding Plaintiffs' current claims regarding prescription opioids. Even in the absence of the allegedly excessive shipments of prescription opioids, substance abuse and the consequences of addiction, damages, and death would have continued to exist. Plaintiffs do not appear to have considered appropriately the constant underlying phenomenon of substance abuse.

(b) Second, prescription opioid misusers, and those diagnosed with opioid abuse or dependence, tend to have certain characteristics that are correlated with substance abuse. As such, these individuals tend to be at increased risk for some form of substance abuse even in the absence of the allegedly excessive shipments.

(c) Third, illicit drug users tend to have certain characteristics that are correlated with substance abuse. These individuals may also be at increased risk for some form of drug abuse even in the absence of the allegedly excessive shipments. Additionally, any connection between the harms associated with fentanyl (including the more powerful fentanyl analogues, such as carfentanil) and the allegedly excessive shipments of prescription opioids by Distributors is highly attenuated and subject to more direct causal factors beyond the responsibility of Distributors. Plaintiffs do not appear to have considered appropriately these issues.

(d) Fourth, substance abuse and its consequences are associated with economic and demographic factors, including declining local industries and limited economic opportunity, that would have continued to exist even in the absence of the allegedly excessive shipments. Plaintiffs do not appear to have considered appropriately these issues.

(e) Fifth, during the period from 2006 to the present, a range of policies were implemented at various levels that were intended to prevent opioid abuse and its associated harms. These policies reflect the recognition that the responsibility for prevention and amelioration extends beyond the suspicious order monitoring obligations of Distributors. As noted above, given the superior information and policy instruments available to other parties, those parties were able to take more comprehensive and sustained action to prevent and ameliorate opioid abuse than was possible through the pharmacy order monitoring activities of Distributors.

(f) Sixth, Ohio Medicaid represents a specific example of a party with better information than Distributors at the patient level, including prescription opioid utilization, as well as the tools to directly limit such utilization. Nonetheless, Ohio Medicaid routinely reimbursed prescription opioid claims for large daily doses and multiple days of supply. To the extent Plaintiffs' characterization of allegedly excessive shipments includes dosage units resulting from prescribing beyond what was strictly medically necessary, Ohio Medicaid had more ability to identify and act on such situations than did Distributors.

242. Accordingly, contrary to the chain of causation articulated by Plaintiffs, Distributors were not the only cause of allegedly excessive shipments of prescription opioids. Further, it is not apparent that allegedly excessive shipments of prescription opioids have led to the claims of harm asserted by Plaintiffs.

B. Drug Abuse as a Long-Term Problem

243. As discussed earlier in this report, substance abuse and addiction have long existed in the U.S. Different drugs have been the focus of enforcement efforts at various times during the past century, including cocaine, heroin, and methamphetamine. Although little statistical evidence exists on the prevalence of illicit drug use over the long term, Exhibit VIII-1 presents a data series beginning in 1979 on the rate of illicit substance use, as self-identified by NSDUH

respondents. It is apparent that during the period prior to the mid-1990s, 6 to 11 percent of individuals admitted to the use of illicit substances at some point in the past year, even excluding marijuana use.

244. Published research has attempted to identify the long-term trend in drug abuse as indicated by the trend in overall drug abuse related mortality. Using data from 1979 to 2016, one study finds that the overall trend in overdose deaths fits an exponential growth curve and that the first half of this curve pre-dates the more widespread impact of prescription opioids.[509] The study concludes: "Although there have been transient periods of minor acceleration or deceleration, the overall drug overdose mortality rate has regularly returned to the exponential growth curve. This historical pattern of predictable growth for at least 38 years strongly suggests that the epidemic will continue along this path for several more years."[510] It is suggested that underlying this trend may be both "push" factors such as economic and technological effects that increase supply, and sociological or psychological "pull" forces that accelerate demand.[511]

245. Information specific to Ohio and the Counties also supports a trend in drug abuse, and identifies additional drugs that are considered to be problematic at various times. For example, the Ohio Department of Health indicates in its 2017 Ohio Drug Overdose Data report that between 2005 and 2017, there was an increase of 1,317 deaths (590 percent increase) involving cocaine, 416 deaths (462 percent increase) involving benzodiazepines, 522 deaths (900 percent increase) involving alcohol, and 3,673 (651 percent increase) involving opioids.[512]

---

509 Jalal, Hawre et al., "Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016," *Science*, 361:6408, September 2018 ("Jalal et al. 2018"), p. 3.

510 Jalal et al. 2018, p. 5.

511 Jalal et al. 2018, p. 5.

512 "2017 Ohio Drug Overdose Data: General Findings," Ohio Department of Health, p. 8, https://odh.ohio.gov/wps/wcm/connect/gov/5deb684e-4667-4836-862b-cb5eb59acbd3/2017_OhioDrugOverdoseReport.pdf?MOD=AJPERES&CONVERT_TO=url&CACHEID=ROOTWORKSPACE.Z18_M1HGGIK0N0JO00QO9DDDDM3000-5deb684e-4667-4836-862b-cb5eb59acbd3-moxPbu6. As a general matter, I understand that attributing death to specific causes, such as an opioid overdose, may depend on the practices used to assign a primary cause of death.

246. The continued use of a range of illicit substances is also evident from the annual reports on Surveillance of Drug Abuse Trends in the State of Ohio published by the Ohio Substance Abuse Monitoring Network ("OSAM"). For example, the January 2000 report for Akron-Canton (including Summit County) cites narcotics officers stating that crack cocaine is a "huge" problem and that "there are more problems caused by people using crack than any other drug."[513] The report later cites law enforcement officers describing methamphetamine as the new number one problem.[514] The section of the January 2000 report dealing with Cuyahoga County notes, similarly: "Crack Cocaine and heroin remain Cuyahoga County's primary drug abuse problem. New user groups of youth abusing heroin and hallucinogens have emerged. Depressants, such as diazepam (Valium) and lorazepam (Ativan) continue to be commonly utilized."[515]

247. Many of the illicit substance abuse trends seen in 2000 remain relevant today, based on more recent OSAM reports. The January 2018 report for Akron-Canton concludes: "Crack cocaine, heroin, marijuana, methamphetamine, and Suboxone remain highly available in the Akron-Canton region; also highly available are fentanyl, Neurontin (gabapentin), powdered cocaine and sedative-hypnotics."[516] The section of the report on the Cleveland region similarly concludes: "Crack cocaine, heroin, marijuana, methamphetamine, Neurontin (gabapentin) and sedative-hypnotics remain highly available in the Cleveland region; also highly available are fentanyl and Suboxone."[517]

---

513 Dickie, Jill L., "Patterns and trends of drug use in Akron and Canton, Ohio," in Ohio Department of Alcohol and Drug Addiction Services, Surveillance of Drug Abuse Trends in the State of Ohio, 2000 ("Dickie 2000"), p. 3.

514 Dickie 2000, p. 8.

515 Koster, Anne, "Patterns and trends of drug use in Cuyahoga County, Ohio," in Ohio Department of Alcohol and Drug Addiction Services, Surveillance of Drug Abuse Trends in the State of Ohio, January 2000 ("Koster 2000"), p. 44.

516 Cummins, Joseph, "Drug Abuse Trends in the Akron-Canton Region," in Ohio Department of Mental Health and Addiction Services, Surveillance of Drug Abuse Trends in the State of Ohio, January 2018 ("Cummins 2018"), p. 53.

517 Sherba, R. Thomas et al., "Drug Abuse Trends in the Cleveland Region," in Ohio Department of Mental Health and Addiction Services, Surveillance of Drug Abuse Trends in the State of Ohio, January 2018 ("Sherba et al. 2018"), p. 124.

248. These trends are indicative of drug abuse being a longer-term problem that did not begin with the wider use of prescription opioids. Further, in light of these trends, a certain amount of drug abuse would be expected in the Counties during the period at issue. Plaintiffs have not identified any increase in drug abuse and related costs that are due to the alleged failures of Distributors with respect to "suspicious" order monitoring.

C. Predisposition to Opioid Misuse

249. Individuals misusing prescription opioids, and those with opioid dependence or abuse conditions, tend to differ systematically from the typical patient prescribed an opioid for pain. I examine survey results from NSDUH and data produced by Ohio Medicaid to explore characteristics associated with the problematic use of opioids. These factors may predispose individuals to some form of substance abuse even in the absence of the allegedly excessive shipments of prescription opioids.

250. The NSDUH (formerly the NHSDA) is an annual survey "sponsored by the Center for Behavioral Health Statistics and Quality (CBHSQ, formerly the Office of Applied Studies) within the Substance Abuse and Mental Health Services Administration (SAMHSA) and is conducted by RTI International."[518] The primary purpose of the survey is "to measure the prevalence and correlates of drug use in the United States."[519] It is a commonly used source in the published literature, including in many of the studies referenced throughout this report. Between 2002 and 2014, the survey asked consistent questions to respondents: whether respondents have ever "used any type of prescription pain reliever that was not prescribed for you or that you took only for the experience or feeling it

---

518 Center for Behavioral Health Statistics and Quality, "2006 National Survey on Drug Use and Health Public Use File Codebook," SAMSHA, Rockville, MD, 2018 ("2006 NSDUH Codebook"), p. i-1.

519 2006 NSDUH Codebook, p. i-1.

caused", as well as their age of first "misuse" along with any misuse that occurred within the previous year.[520]

251. The NSDUH asks additional questions to impute whether a respondent suffers from opioid abuse or dependence. Opioid dependence is defined as meeting at least three of seven criteria.[521] Opioid abuse is defined as meeting one or more of four criteria.[522] The NSDUH does not allow a respondent to have both opioid abuse and dependence. In addition, the survey also asks about heroin use, imputing heroin abuse and dependence in the same manner.

252. Exhibit VIII-2 shows the national percentage of the population misusing prescription pain relievers, according to the NSDUH, as well as the percentage of the population classified with opioid abuse or dependence.[523] Prescription pain reliever misuse was relatively constant at 4 to 4.4 percent between 2002 and 2010,

---

520 Center for Behavioral Health Statistics and Quality, "2006 National Survey on Drug Use and Health: CAI Specs for Programming; English Version," SAMSHA, Rockville, MD, 2005, pp. 126-128. I restrict this analysis to the period 2002 through 2014 because this period is not associated with any changes to either the survey sampling methodology or the wording of the relevant questions.

521 The criteria are: "(1) Spent a great deal of time over a period of a month getting, using, or getting over the effects of the substance[;] (2) Unable to keep set limits on substance use or used more often than intended[;] (3) Needed to use substance more than before to get desired effects or noticed that using the same amount had less effect than before[;] (4) Unable to cut down or stop using the substance every time he or she tried or wanted to[;] (5) Continued to use substance even though it was causing problems with emotions, nerves, mental health, or physical problems[;] (6) Reduced or gave up participation in important activities due to substance use[;…] (7) experienced substance specific withdrawal symptoms at one time that lasted for longer than a day after they cut back or stopped using" (2006 NSDUH Codebook, p. 249). In addition, the criteria for opioid dependence are "not considered to be met for those individuals taking opioids solely under appropriate medical supervision" (see https://www.asam.org/docs/default-source/education-docs/dsm-5-dx-oud-8-28-2017.pdf?sfvrsn=70540c2_2).

522 The criteria are: "(1) Respondent reported having serious problems due to substance use at home, work or school[;] (2) Respondent reported using substance regularly and then did something where substance use might have put them in physical danger[;] (3) Respondent reported substance use causing actions that repeatedly got them in trouble with the law[;] (4) Respondent reported having problems caused by substance use with family or friends and continued to use substance even though it was thought to be causing problems with family and friends" (2006 NSDUH Codebook, p. 251).

523 The prescription pain relievers referred to are predominantly opioids; see Ahrnsbrak, Rebecca et al., "Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health," SAMHSA, 2017, Table A.12B, https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.htm#taba12b.

declining to an average of 3.5 percent between 2011 and 2014.[524] Rates of prescription pain reliever abuse and dependence are lower, never exceeding more than 0.6 percent of the population.

253. Exhibit VIII-3 examines the characteristics of prescription pain reliever misusers relative to respondents who had not misused prescription pain relievers or heroin, according to the NSDUH survey results. Prescription pain reliever misusers are less likely to be female: 44.6 percent as compared to 52.1 percent for those who had not misused prescription pain relievers or heroin. Prescription pain reliever misusers are also less educated: 18.1 percent of prescription pain reliever misusers graduated college or university compared to 27.8 percent for the rest of the population. In addition, prescription pain reliever misusers were more likely than those who had not misused prescription pain relievers and heroin to have used other illicit substances prior to misusing prescription pain relievers. These differences all are statistically significant at the five percent level.

254. Data from Ohio Medicaid include health records and prescription claims for all Medicaid enrollees in the Counties between 2010 and 2017 (including those receiving treatment in the Counties) who: (i) received an opioid prescription; (ii) received a prescription for naloxone, naltrexone, and/or buprenorphine; and/or (iii) were diagnosed with an ICD code associated with opioid abuse or dependence. Using these data, I am able to follow the medical and prescription history of these individuals over time so long as they remained enrolled in Medicaid.

255. I select those beneficiaries who would appear to have received their "first" prescription of opioids within the window of the data provided.[525] Exhibit VIII-4 shows that in any of the three years after the "first" opioid prescription (as defined

---

524 See also Kandel, Denise B., et al., "Increases from 2002 to 2015 in prescription opioid overdose deaths in combination with other substances," *Drug Alcohol Dependence*, 178, 2017, p. 501.

525 I define an opioid prescription as a patient's "first" if it is preceded by at least one full year in which the patient received no opioid prescription and the patient did not have a prior "first" opioid prescription.

above), the likelihood of an Ohio Medicaid recipient receiving an opioid abuse or dependence diagnosis is less than 1 percent. Accordingly, it would appear that the vast majority of Ohio Medicaid recipients who received their "first" opioid prescription did not go on to receive an opioid abuse or dependence diagnosis.[526]

256. Exhibit VIII-5 presents my analysis of the likelihood that Ohio Medicaid recipients with certain medical conditions[527] prior to their "first" opioid prescription would develop an opioid use disorder within each of the first three years following the prescription. The results are presented in the form of odds ratios comparing the likelihood of an opioid abuse or dependence diagnosis among those with the specified condition as compared to those without the condition. For example, an odds ratio of 3 indicates that an Ohio Medicaid recipient with the medical condition at issue was three times as likely to develop an opioid use disorder as an Ohio Medicaid recipient without the medical condition. As is apparent, various prior medical conditions have a strong effect on the likelihood of developing an opioid use disorder, including diagnosed alcohol abuse, anxiety disorder, bipolar disorder, depression, post-traumatic stress disorder ("PTSD"), and schizophrenia.

257. These results are generally consistent with a recent study of Medicaid enrollees in Rhode Island, which examined the factors that could be used to predict future opioid dependence, abuse, or poisonings (i.e., overdose) based on information available as of the individual's initial opioid prescription.[528] The study finds that individual characteristics associated with the highest relative risks of adverse outcomes are release from a corrections facility, compulsive disorders, and prior prescriptions for atypical antipsychotics, centrally-acting muscle relaxants, benzodiazepines, and opiate agonists (such as cough syrups and mild pain

---

526 For a related finding, see Higgins, C. et al., "Incidence of iatrogenic opioid dependence or abuse in patients with pain who were exposed to opioid analgesic therapy: a systematic review and meta-analysis," *British Journal of Anaesthesia*, 120:6, 2018, p. 1335.

527 Medical conditions are determined based on diagnoses as recorded in the Ohio Medicaid Data.

528 Hastings, Justine S. et al., "Predicting High-Risk Opioid Prescriptions Before they are Given," NBER Working Paper 25791, April 2019 ("Hastings et al. 2019"), p. 1.

medications).[529] Additional significant predictors are social factors such as household size and the statewide monthly unemployment rate.[530]

258. From these analyses, I note that it would appear to be a small percentage of those prescribed opioids that then develop an opioid use disorder. Further, it is apparent that various causal factors relating to an individual's predisposition to drug abuse are relevant in determining whether the misuse or abuse of opioids would result from a prescription for opioids. These factors would have been operational even if Distributors had reported and/or blocked a greater number of "suspicious" orders.

D. The Claimed Transition to Illicit Opioids

259. Plaintiffs suggest that the conduct of Distributors set the stage for a significant increase in demand for illicit opioids during the period following 2010.[531] Nonetheless, I note that the prevalence of illicit opioid use has been, and remains low.[532]

260. Trends in mortality rates associated with opioids for the Counties are presented in Exhibits VIII-6 and VIII-7 for the period 1999 through 2016. Three episodes are evident in the trends. Overdose mortality rates specific to prescription opioids increased in the Counties until approximately 2011 and have declined since then in Cuyahoga County, with an apparent increase in 2016 in Summit County. Mortality rates from heroin increased until approximately 2013 and have apparently declined since then. Since approximately 2013, mortality rates associated with synthetic opioids (including fentanyl) have risen rapidly. It is noted that in Cuyahoga County, officials are finding that dealers are increasingly mixing cocaine with fentanyl; more people are dying using cocaine-fentanyl

529 Hastings et al. 2019, p. 6.

530 Hastings et al. 2019, p. 30.

531 Summit Complaint, ¶¶ 6, 1057; Cuyahoga Complaint, ¶¶ 6, 1087; Gruber Report, ¶ 16.

532 See e.g., "Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health," U.S. Department of Health and Human Services' ("HHS") Publication No. SMA 18-5068, NSDUH Series H-53, Center for Behavioral Health Statistics and Quality, SAMHSA, 2018, Table A.10B.

mixtures than cocaine-heroin mixtures. As such, it is not apparent that recent deaths associated with illicit fentanyl use were among individuals seeking to use opioids illicitly.[533]

261. It not apparent that the trend in mortality rates associated with the use of illicit opioids is a useful metric for opioid related harms for which Distributors are allegedly responsible. As noted earlier in this report, rates of opioid misuse, abuse, and dependence have been flat or declining. In contrast, total deaths from drug overdoses increased in Ohio between 2012 and 2017, as shown in Exhibit VIII-8. As discussed in greater detail below, one reason for the increase in mortality has been the increase in the lethality of illicit opioids, particularly those that are cut with fentanyl (including its analogue, carfentanil), significantly more powerful and significantly cheaper to produce than heroin.

(a) Estimates of the Extent of Transition to Illicit Opioids

262. The available information addresses the transition to illicit opioid use among prescription opioid misusers; it does not address the incidence of illicit opioid use among patients new to prescription opioids. Even among those misusing prescription opioids, this transition is rare; according to one study, only 3.6 percent of non-medical users of opioids initiated heroin use within five years of first non-medical opioid use.[534] Further, as discussed above, only a minority of opioid misusers started with a prescription for opioids.[535] Recently published data also indicate that an increasing number of heroin users have initiated their use of heroin without first misusing prescription opioids, accounting for nearly one third

---

533 MacDonald, Evan, "Why cocaine is setting off alarm bells for federal and state drug enforcers in Northeast Ohio," *Cleveland.com*, March 27, 2019, https://www.cleveland.com/news/2019/03/why-cocaine-is-setting-off-alarm-bells-for-federal-and-state-drug-enforcers-in-northeast-ohio html.

534 Muhuri, Pradip K. et al., "Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States," SAMHSA Center for Behavioral Health Statistics and Quality Data Review, August 2013, p. 14. See also Compton et al. 2016, p. 160: "Yet, although the majority of current heroin users report having used prescription opioids nonmedically before they initiated heroin use, heroin use among people who use prescription opioids for nonmedical reasons is rare, and the transition to heroin use appears to occur at a low rate."

535 Singer et al. 2019, p. 618.

of heroin initiates in 2015.[536] As noted by Lou LaMarca, Clinical Director of Community Assessment and Treatment Services for Cuyahoga County, it is "rare" for an individual receiving addiction treatment services "to have started with a medically necessary opioid" prescription.[537]

263. Published estimates also suggest that among those using prescription opioids non-medically, less than 1 percent report ever having used heroin.[538] Since it is only a minority of those prescribed opioids who engage in at least opioid misuse in the broadest sense (i.e., use opioids contrary to directions, even if for the purposes of pain relief), the rate of transition from medical use of prescription opioids to heroin must accordingly be substantially less than 1 percent.[539]

(b) Demographic Differences

264. In contrast to the transitional or gateway theory advanced by Plaintiffs, it appears that heroin users represent a subgroup of the population that differs in important ways from the typical patient prescribed an opioid. These differences would appear to be inconsistent with a theory of causation running from the medical use of prescription opioids to illicit opioid use.

(a) According to data published by the CDC, patients prescribed an opioid in 2011-2012 were more likely to be women than men and were more likely to be in the 40-59 age category than 20-39 or 60+.[540] According to the Ohio Medicaid Data, the median age of Ohio Medicaid recipients "first"

536 Cicero, Theodore J. et al., "Increased use of heroin as an initiating opioid of abuse: Further considerations and policy implications," *Addictive Behaviors*, 87, 2018 ("Cicero et al. 2018"), p. 267.

537 Deposition of Lou LaMarca, Clinical Director at Community Assessment & Treatment Services, March 22, 2019, p. 86; CUYAH_002048206–07.

538 Evans et al., "How the Reformulation of OxyContin Ignited the Heroin Epidemic," *Review of Economics and Statistics*, 101(1), 2019 ("Evans et al. 2019"), p. 5.

539 See Vowles et al. 2015, p. 569.

540 "Prescription Opioid Analgesic Use Among Adults: United States, 1999-2012," National Center for Health Statistics Data Brief No. 189, CDC, February 2015, p. 3.

prescribed an opioid in 2011 through 2017 is between 27 and 40; between 50.4% and 65.1% percent were female in each year.[541]

(b) In contrast, the CDC's Annual Surveillance Report for 2016 indicates that well over half of those initiating heroin use in 2016 were 25 and under.[542] Of those visiting emergency departments for heroin poisoning (i.e., overdose) in 2015, over two-thirds were male and over two-thirds were 34 or under.[543] According to a study based on NSDUH data collected from 2004 to 2011, the peak period of heroin initiation occurs at ages 17-18; prior non-medical opioid use is associated with heroin initiation, with the highest risk among those who first misused opioids aged 10-12.[544]

265. Using the NSDUH Data, I explore the supposed transition from prescription opioid misuse to heroin use by comparing prescription pain reliever misusers who went on to use heroin to respondents who misused prescription pain relievers but never used heroin. These results are presented in Exhibit VIII-9. Plaintiffs allege that it was prescription opioids that led to individuals using heroin. If so, I would expect that there should be little difference in the characteristics of those who misused prescription pain relievers and then used heroin as compared to those who misused prescription pain relievers but have not used heroin. The exhibit, however, shows that contrary to Plaintiffs' allegations, there are significant differences in the two groups. Compared to heroin users, those who misused prescription pain relievers but have not used heroin are more likely to be female and more educated, with the differences statistically significant at the five percent level.

---

541 See Backup Materials.

542 "2018 Annual Surveillance Report of Drug-Related Risks and Outcomes: United States," CDC ("CDC 2018 Surveillance Report"), Table 2D, p. 56.

543 CDC 2018 Surveillance Report, Table 3A, p. 59.

544 Cerda, Magdalena et al., "Nonmedical Prescription Opioid Use in Childhood and Early Adolescence Predicts Transitions to Heroin Use in Young Adulthood: A National Study," *Journal of Pediatrics*, 167:3, 2015, p. 605.

266. The demographic and addiction characteristics of fentanyl overdose victims show greater comparability with heroin users than with patients prescribed opioids.

(a) A study published by the CDC notes that from 2011 to 2016, "[t]he rate of drug overdose deaths involving fentanyl increased exponentially for both sexes, with the rate increasing more rapidly for males than for females. Rates also increased exponentially across all age groups, with the greatest increases among those aged 15–24 and 25–34."[545]

(b) According to a study of fentanyl overdose incidents in Ohio, "the demographic of fentanyl decedents in Ohio closely matched those of heroin overdose decedents, but diverged from prescription opioid overdose decedents."[546] The study also observes:

> In Ohio's 14 high-burden counties, 56% of fentanyl deaths tested positive for heroin or cocaine in 2014, with 39% testing positive for heroin and 23% for cocaine (Table 2). … Other characteristics of fentanyl deaths included current diagnosed mental health disorder (25%) and recent release (within 30 days) from a jail, hospital, or treatment facility (10.3%).[547]

(c) Supply Conditions

267. As one study concludes, "taken in total, the available data suggest that nonmedical prescription-opioid use is neither necessary nor sufficient for the initiation of heroin use and that other factors are contributing to the increase in the rate of heroin use and related mortality."[548] Among these other factors are the cost and availability of the illicit substances. For example, the study cited above notes: "The price in retail purchases has been lower than $600 per pure gram every year since 2001, with costs of $465 in 2012 and $552 in 2002, as compared

---

545 Spencer, Merianne Rose et al., "Drug Overdose Deaths Involving Fentanyl, 2011-2016," *National Vital Statistics Reports*, 68:3, 2019, p. 5.

546 Peterson, Alexis B. et al., "Increases in Fentanyl-Related Overdose Deaths – Florida and Ohio, 2013-2015," *Morbidity and Mortality Weekly Report*, CDC, 65:33, 2016 ("Peterson et al. 2016"), p. 847.

547 Peterson et al. 2016, p. 846.

548 Compton et al. 2016, p. 158. See also Wichern Report, Section IV.

with $1237 in 1992 and $2690 in 1982."[549] Another study cited extensively by Plaintiffs' experts notes: "Over the past thirty years, there has been an increasing supply of heroin from Mexican gangs. … The price fell from more than $3,000 per pure gram in 1981 to less than $500 in 2012."[550] Most of this price decline occurred prior to 1998.[551] Furthermore, it has been found that from 1992 to 2008, each $100 decrease in the price per gram of heroin resulted in a 2.9 percent increase in the number of heroin overdose hospitalizations.[552]

268. Plaintiffs and their experts attempt to interpret these events as a manifestation of increasing "thickness" in the markets for illicit opioids. As characterized in the Gruber Report: "The increase in demand, in turn, induces existing dealers to expand their existing operations and expand into new areas, and induces new entry into the marketplace."[553] Underlying this thick markets conjecture appears to be a change in market structure in which heroin supply became more competitive in response to demand created by prescription opioid misuse.

269. This conjecture continues to require an increase in demand for illicit opioids caused by substitution from prescription opioids, as in the transition theory discussed above;[554] accordingly, it is subject to the same criticisms articulated above. Moreover, I am not aware of any supporting information from Plaintiffs for the proposition that heroin supply underwent a transition from a less competitive to a more competitive market structure as a consequence of demand generated by prescription opioid misuse; Plaintiffs' expert, Professor Cutler, admits that no data are available to support such a contention.[555]

---

549 Compton et al. 2016, p. 158.

550 Evans et al. 2019, p. 5. See also Cutler Report, fn. 35, 37, 39, 41, 49, 70; Gruber Report, fn. 72, 96, 118.

551 Evans et al. 2019, supplementary appendix, Figure C2.

552 Unick, George et al., The relationship between US heroin market dynamics and heroin-related overdose, 1992–2008," *Addiction*, 109:11, 2014, p. 1889.

553 Gruber Report, ¶ 66. See also Cutler Deposition Day 1, pp. 321-325, 357, 360-362.

554 See e.g., Deposition of David Cutler, Ph.D., April 27, 2019 ("Cutler Deposition Day 2"), pp. 428-429, 437.

555 See Cutler Deposition Day 1, p. 361; Cutler Deposition Day 2, pp. 412-414; 450-452.

270. In contrast, information does exist that is contrary to this conjecture. Heroin prices observed in the post-2010 period are part of a steady decline that began in the early 1980s,[556] a trend apparently unconnected with prescription opioids. A simpler explanation for this phenomenon and consistent with the Evans et al. 2019 article cited heavily by Plaintiffs' experts is that the heroin supply has gradually increased over time, resulting in a gradual decline in price. As one article summarizes: "the increase in the rates of heroin use preceded changes in prescription-opioid policies, and there is no consistent evidence of an association between the implementation of policies related to prescription opioids and increases in the rates of heroin use or deaths, although the data are relatively sparse."[557]

271. Supply factors apply to both heroin and fentanyl, but are especially pronounced in relation to fentanyl and its analogues, including carfentanil. Since 2013, fentanyl availability has increased dramatically, with a corresponding decline in cost. Most illicit fentanyl is manufactured in China and is typically sent directly to the U.S. or sent to Canada or Mexico and smuggled into the U.S.[558] According to one estimate, fentanyl seizures increased 1,400 percent from 2013 to 2015; nonetheless, at least 134 kilograms of pure fentanyl are estimated to have entered the U.S. in 2016, enough for 134 to 536 million doses.[559]

272. Prices of fentanyl are low relative to heroin on a per kilogram basis. According to a 2017 study, heroin was available at $65,000 per kilogram wholesale, compared to $3,500 per kilogram for fentanyl.[560] Nonetheless, illicit fentanyl appears to be extremely profitable. According to the DEA, a $1,000 investment in the

---

556 Evans et al. 2019, p. 5.

557 Compton et al. 2016, p. 160.

558 "National Drug Threat Assessment," DEA, October 2018, https://www.dea.gov/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20final%20low%20resolution.pdf.

559 Ciccarone, Daniel, editorial for "US Heroin in Transition: Supply Changes, Fentanyl Adulteration and Consequences," *International Journal of Drug Policy*, 46, 2017, p. 3.

560 Frank, Richard G. and Harold A. Pollack, "Addressing the Fentanyl Threat to Public Health," *New England Journal of Medicine*, 376:7, 2017, p. 605.

production of heroin may realize revenues between $3,000 and $5,000; in contrast, a $1,000 investment in the production of illicit fentanyl may realize revenues of approximately $1.5 million.[561]

(d) Fentanyl Lethality

273. A key element considered in CDC research is the "mixing of fentanyl into the heroin supply by drug traffickers and persons misusing opioids."[562] It is further observed that the "high potency and rapid action onset of fentanyl and fentanyl analogs and the difficulty of mixing nonlethal doses makes fentanyl more dangerous to use than heroin."[563] Additionally, deaths involving illicitly manufactured fentanyl are driven in part by the rapid evolution of products containing illicitly manufactured fentanyl, which is "distributed in counterfeit prescription pills [], mixed with and sold as cocaine, or sold as powders to persons using heroin with and without their knowledge that the product contains fentanyl."[564]

274. Recent findings on increased heroin initiation without any prior opioid misuse, as discussed above, are also relevant in understanding the potential drivers of fentanyl-related mortality.

> [I]t cannot be denied that new initiates to opioid use through heroin are at increased risk of overdose than those with prior experience to prescription opioid [sic] due to a number of factors: 1) as opposed to prescription pills with marked dosage, heroin typically has a purity unknown to the user; 2) additives such as the far cheaper fentanyl and its dangerous analogues (e.g., carfentanil) may be mixed with the heroin; 3) estimating the dose is difficult for even experienced users; and 4) an opioid naïve individual who has not yet become tolerant to opioids may be at risk of overdose

561 "2017 National Drug Threat Assessment Summary," DEA, October 2017, https://www.dea.gov/documents/2017/10/01/2017-national-drug-threat-assessment.

562 O'Donnell, Julie K. et al., "Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region - United States, 2006-2015," *Morbidity and Mortality Weekly Report*, CDC, 66:34, 2017 ("O'Donnell et al. 2017") p. 901. As noted above, fentanyl has been found mixed into other non-opioids as well.

563 O'Donnell et al. 2017, p. 901.

564 O'Donnell et al. 2017, p. 902.

> with even a singular exposure due a combination of one or more of these factors. The risk of overdose is thus markedly higher in these new users than it would be in maximally tolerant, long-term users. This may account for the rapidly escalating number of overdose deaths experienced in recent years[.][565]

275. Exhibit VIII-10 shows that between 2002 and 2010, the average annual growth rates of opioid use disorder and heroin-related mortality were 3 percent and 5 percent, respectively. Starting in 2010, however, a divergence took place. Between 2011 and 2016, the average annual growth rates of opioid use disorder and heroin-related mortality were 1 percent and 29 percent, respectively. If the increase in heroin-related mortality were driven entirely by the alleged shift of prescription opioid misusers to heroin, then one would expect the relative growth rates of opioid use disorder and heroin-related mortality to be approximately identical before and after 2010, but this is not what is observed. In contrast, the substantially higher growth rate of heroin-related mortality post-2010 is consistent with the introduction of a deadlier form of the drug; namely, as discussed above, heroin laced with illicit forms of fentanyl.

276. Consequently, it is apparent that various causal factors relating to the prevalence of illicit opioid use are relevant in determining the extent of any harms from that use. These factors would have been operational even if Distributors had reported and/or blocked a greater number of "suspicious" orders.

E. The Role of Economic Conditions

277. Several recent research papers have addressed the relationship between opioid misuse and/or opioid use disorders in a region and the state of the region's economy. Much of this research has been motivated by the observation of a "marked deterioration in the morbidity and mortality of middle-aged white non-Hispanics in the United States after 1998."[566] This trend has been referred to as

---

565 Cicero et al. 2018, p. 269.

566 Case, Anne, and Angus Deaton, "Rising Morbidity and Mortality in Midlife Among White non-Hispanic Americans in the 21st century," *Proceedings of the National Academy of Sciences*, 112:49, 2015, p. 15078.

"Deaths of Despair", encompassing deaths due to drugs, alcohol, and/or suicide.[567] The increases in mortality are concentrated among those without a college degree and with lower incomes, suggesting that "Deaths of Despair" are the result of "a long-standing process of cumulative disadvantage for those with less than a college degree."[568] This "cumulative disadvantage" includes a lower probability of finding a high-paying job, lower probability of marriage, lower probability of children, and an increased probability of health/mental health problems.[569]

278. Related research finds a strong correlation between the opioid prescriptions written in an area and the area's socioeconomic characteristics, which also tend to drive the social services needs and burdens associated with the area. Generally, higher levels of prescription opioid utilization are correlated with poorer economic outcomes such as lower wages, an increased probability of being unemployed, lower socioeconomic status such as lower education levels, and demographics such as race and gender. For example, one study finds that the quantity of opioids prescribed in a county is positively correlated with the percentage of people below the poverty line and the number of uninsured.[570] Another finds that both medical and non-medical prescription opioid use are positively correlated with poverty and unemployment rates, and that these effects were especially pronounced in the Midwest and Appalachian regions.[571]

279. Several studies attempt to estimate more directly whether (and how) changes in economic conditions cause changes in opioid use and misuse. Some research has found that changes in economic conditions do cause changes in opioid use and misuse. According to this research, negative economic shocks to a region cause

---

567 Case, Anne, and Angus Deaton, "Mortality and Morbidity in the 21st century," Brookings Papers on Economic Activity, 2017 ("Case and Deaton 2017"), p. 398.

568 Case and Deaton 2017, p. 397.

569 Case and Deaton 2017, pp. 413-416.

570 McDonald, Douglas C. et al., "Geographic Variation in Opioid Prescribing in the US," *The Journal of Pain*, 13:10, 2012, pp. 988-996.

571 Ghertner, Robin, and Lincoln Groves, "The Opioid Crisis and Economic Opportunity: Geographic and Economic Trends," *ASPE Research Brief*, 2018.

an increase in opioid use and/or opioid-related mortality and morbidity. Some representative and statistically significant findings include:

(a) Increases in county unemployment lead to increases in opioid-related mortality and morbidity;[572]

(b) Increases in state-level unemployment lead to increases in opioid abuse;[573]

(c) Declines in manufacturing employment in a county lead to increases in opioid use and opioid-related mortality in the county;[574] and

(d) Increases in trade with China in highly "exposed" counties lead to increases in opioid-related mortality in those counties.[575]

280. One study specifically addresses circumstances in Ohio, noting that the geographic distribution of opioid overdoses within Ohio is uneven.[576] The study goes on to note: "Opioid dependence and abuse results from a complex set of social, health, and economic factors."[577] The authors estimate a regression model of county-level (total) opioid overdose mortality rates in 2015 on several economic, demographic, and health factors. Notable statistically significant findings include:[578]

(a) A higher county unemployment rate is associated with higher overdose death rates;

---

572 Hollingsworth, Alex, et al., "Macroeconomic Conditions and Opioid Abuse," *Journal of Health Economics*, 56, 2017 ("Hollingsworth et al. 2017"), pp. 222-233.

573 Carpenter, Christopher S. et al., "Economic Conditions, Illicit Drug use, and Substance use disorders in the United States," *Journal of Health Economics*, 52, 2017 ("Carpenter et al. 2017"), pp. 63-73.

574 Charles, Kerwin Kofi, et al., "The Transformation of Manufacturing and the Decline in U.S. employment," *NBER Macroeconomics Annual 2018*, 33, 2018 ("Charles et al. 2018").

575 Pierce, Justin R. and Peter K. Schott, "Trade Liberalization and Mortality: Evidence from US counties," National Bureau of Economic Research, No. 22849, 2018 ("Pierce and Schott 2018").

576 Rembert, Mark et al., "Taking Measure of Ohio's Opioid Crisis," Ohio State University, Swank Program in Rural-Urban Policy, October 2017 ("Rembert et al. 2017"), pp. 3-4.

577 Rembert et al. 2017, p. 10.

578 Rembert et al. 2017, pp. 10-14.

(b) A larger decline in manufacturing employment during the 2007-2010 recession is associated with higher overdose death rates;

(c) A higher poverty rate in 2010 was associated with higher overdose death rates;

(d) Fewer economic opportunities (measured in terms of county-level intergenerational mobility) are associated with higher overdose death rates; and

(e) Higher opioid prescriptions per capita are associated with higher overdose death rates.

281. In general, the available results suggest that measures of economic decline are relevant in understanding the impact of opioid misuse and abuse. I note that the Expert Report of Kevin Murphy, Ph.D., dated May 10, 2019 ("Murphy Report"), also indicates that opioid abuse and other health and economic outcomes reflect many factors, including the long-run process of economic decline that has affected certain regions of the U.S., Ohio, and the Counties in particular.[579]

282. Consequently, it is apparent that various economic factors underlie opioid misuse and/or abuse. These factors must be considered in determining the extent of any resulting harms as they would have been operational even if Distributors had reported and/or blocked a greater number of "suspicious" orders.

F. Preventive Policy Interventions

283. During the period of the alleged conduct, many jurisdictions enacted policies designed to limit the availability of prescription opioids. In many cases, these policy initiatives are associated with improved outcomes with respect to prescription opioid misuse, again indicating that opioid related harms are driven

[579] Murphy Report, ¶¶ 18a, 18b.

by multiple factors, many of which are not under the direct control of Distributors.

(a) More Restrictive Prescribing Guidelines

284. As discussed earlier in this report, the period at issue saw the introduction of several guidelines designed to establish best practices regarding the use of opioids. It is believed that the CDC Guidelines were directly responsible for the implementation of state laws restricting opioid dosing, as well as measures taken by health insurers to implement limits to MME for chronic pain.[580] Academic research has also addressed whether the introduction of guidelines had any impact on the opioid prescribing behavior of physicians.

(a) A study at the University of Michigan hospital found a statistically significant decrease in both the median prescription amount and the total number of opioid prescriptions for laparoscopic cholecystectomy following implementation of postoperative prescription guidelines.[581]

(b) Similarly, another study focusing on hand and gallbladder surgeries found that the introduction of guidelines for post-operative pain led to a substantial and statistically significant reduction in opioid prescriptions for two types of surgery and statistically insignificant decreases in opioid prescriptions for two other types of surgeries.[582]

(c) Additionally, a study has addressed the impact of guidelines designed for Washington State public payors.[583] The guidelines were instituted in 2007. Using Washington State workers' compensation claims, the authors

---

580 Schatman et al. 2019, pp. 650-651.

581 Howard, Ryan, Jennifer Waljee, Chad Brummett, Michael Englesbe, and Jay Lee, "Reduction in Opioid Prescribing through Evidence-Based Prescribing Guidelines," *JAMA surgery*, 153:3, 2018 ("Howard et al. 2018"), pp. 285-287.

582 Stanek, Joel J et al., "The Effect of an Educational Program on Opioid Prescription Patterns in Hand Surgery: a quality improvement program," *The Journal of hand surgery*, 40:2, 2015, p. 344.

583 Franklin, Gary M. et al, "Bending the Prescription Opioid Dosing and Mortality Curves: Impact of the Washington State Opioid Dosing Guideline," *American Journal of Industrial Medicine*, 55, 2012 ("Franklin et al. 2012).

show that starting in 2009 (and a lesser extent 2008), the average daily MME dose prescribed for schedule II, III, and IV controlled substances began to decline as did the number of workers who claimed at least one opioid prescription. Furthermore, 2010 worker compensation opioid-related deaths dropped significantly from the previous year.[584]

(b) Prescription Drug Monitoring Programs

285. Originally, studies of PDMPs found that the programs had little apparent effect on the supply of opioids or opioid-related mortality and morbidity.[585] Recently, researchers have criticized these early studies for failing to adequately distinguish between PDMPs which make it mandatory for prescribers and/or pharmacists to access the PDMP and look up a patient's history before writing or dispensing an opioid prescription (a "mandate") versus those that do not. Once the characteristics of each state's PDMP are taken into account, PDMPs with a mandate (such as OARRS in Ohio) appear to result in decreases in opioid prescribing, doctor shopping, crime, and the number of foster children.[586]

---

584 Franklin et al. 2012, pp. 327-328.

585 See, for example, Li, Guohua et al., "Prescription Drug Monitoring and Drug Overdose Mortality," *Injury Epidemiology*, 1:1, 2014; Brady, Joanne E.et al., "Prescription Drug Monitoring and Dispensing of Prescription Opioids," *Public Health Reports*, 129:2, 2014, pp. 139-147; Paulozzi, Leonard J. et al., "Prescription Drug Monitoring Programs and Death Rates From Drug Overdose," *Pain Medicine*, 12:5, 2011, pp. 747-754; Moyo, Patience et. al., "Impact of Prescription Drug Monitoring Programs (PDMPs) on Opioid Utilization among Medicare Beneficiaries in 10 US States," *Addiction*, 112:10, 2017, pp. 1784-1796.

586 Researchers have examined the impact of PDMPs on criminal activity (Dave, Dhavalet al., "Prescription Drug Monitoring Programs, Opioid Abuse, and Crime," No. w24975, National Bureau of Economic Research ("NBER"), 2018 ("Dave et al. 2018")); foster care services (Gihleb, Rania et al., "The Effects of Mandatory Prescription Drug Monitoring Programs on Foster Care Admissions," 2018; Grecu, Anca M. et al., "Mandatory access prescription drug monitoring programs and prescription drug abuse," *Journal of Policy Analysis and Management*, 38:1, 2019 ("Grecu et al. 2019"), pp. 181-209); opioid misuse and diversion (Buchmueller, Thomas C., and Colleen Carey, "The effect of Prescription Drug Monitoring Programs on Opioid Utilization in Medicare," No. w23148, NBER, 2017 ("Buchmueller and Carey 2017"); Grecu et al. 2019; Bao, Yuhua et al., "Assessing the Impact of State Policies for Prescription Drug Monitoring Programs on High-Risk Opioid Prescriptions," *Health Affairs*, 37:10, 2018, pp. 1596-1604; Meinhofer, Angelica, "Prescription drug monitoring programs: The role of asymmetric information on drug availability and abuse," *American Journal of Health Economics*, 4:4, 2018 ("Meinhofer 2018"), pp. 504-526; Ali et al., "Prescription drug monitoring programs, nonmedical use of prescription drugs, and heroin use: Evidence from the National Survey of Drug Use and Health, *Addictive Behaviors*, 69, ("Ali et al. 2017"), pp. 65-77; Mallatt, Justine, "The effect of Prescription Drug Monitoring Programs on opioid prescriptions and heroin crime rates," 2017 ("Mallatt 2017")); and

286. Accordingly, PDMPs that are effective at reducing diversion and prescription opioid-related mortality and morbidity are those which make it mandatory for prescribers (or pharmacies) to consult a PDMP before writing (or filling) an opioid prescription. As of January 2019, 43 states had PDMPs with mandates in place;[587] however, PDMPs with these characteristics are a relatively recent phenomena. By the end of 2013, only 10 states, including Ohio, had PDMPs with mandates in place.[588]

(c) Pain Management Clinic Laws

287. PMCLs are state-level programs designed to prevent or reduce instances in which PMCs are a source of prescription opioid diversion. Research has found that PMCLs are generally effective at reducing the number of opioid prescriptions, the level of opioid misuse, and opioid-related mortality,[589] even after accounting for the implementation of PDMPs.[590]

288. Consequently, it is apparent that various causal factors relating to policies adopted by various government agencies were relevant in determining the extent of any harms resulting from opioid misuse and/or abuse. Effective preventive efforts have aimed at prescribing practices, underlining that causation is tied to prescriptions. These factors would have been operational even if Distributors had reported and/or blocked a greater number of "suspicious" orders.

---

time spent on disability (Savych, Bogdan et al., "Do Opioids Help Injured Workers Recover and Get Back to Work? The Impact of Opioid Prescriptions on Duration of Temporary Disability," No. w24528, NBER, 2018).

587 PDMP Training and Technical Assistance Center, "Mandatory Query by Prescribers and Dispensers," http://www.pdmpassist.org/pdf/Mandatory_Query_20190115.pdf.

588 Buchmueller and Carey 2017, p. 31.

589 See, for example, Meinholder, Angelica, "The War on Drugs: Estimating the Effect of Prescription Drug Supply-Side Interventions," Brown University, 2015; Mallatt 2017, p. 19; Lyapustina, Tatyana et al., "Effect of a 'pill mill' law on opioid prescribing and utilization: The case of Texas," *Drug Alcohol Depend*, 159, 2016, p. 7, for the impact on opioid prescriptions. See Surratt, Hilary L. et al., "Reductions in prescription opioid diversion following recent legislative interventions in Florida," *Pharmacoepidemiology and Drug Safety*, 23, 2014, addressing the level of opioid misuse; and Kennedy-Hendricks, Alene et al., "Opioid Overdose Deaths and Florida's Crackdown on Pill Mills," *AJPH*, 106:2, 2016, p. 295; and Deiana and Giua 2018 for the impact of PMCLs on opioid-related mortality.

590 See, for example, Mallatt 2017; Deiana and Giua 2018.

G. Ohio Medicaid

289. The Medicaid program provides health insurance to certain categories of low-income families and individuals.[591] Medicaid is funded jointly by federal and state governments, but "[e]ach state establishes its own eligibility standards, benefits package, payment rates and program administration under broad federal guidelines."[592] While state Medicaid programs are not required by law to cover prescription drugs,[593] all states have long provided prescription drug coverage to at least some categories of Medicaid-eligible residents.[594]

290. Medicaid covers most outpatient prescription drugs, provided these are obtained from participating providers (pharmacies or physicians).[595] Under the Omnibus Budget Reconciliation Act of 1990 ("OBRA 90"), states had to reimburse for all "covered outpatient drugs of any manufacturer which has entered into and complies with an agreement under section 1927(a), which are prescribed for a medically accepted indication."[596] Further legislation enacted in 1993 permitted states to implement restrictive formularies[597] by excluding covered drugs, subject to certain requirements, namely that "the excluded drug does not have a significant, clinically meaningful therapeutic advantage … over other drugs

---

591 "A Profile of Medicaid: Chartbook 2000," Health Care Financing Administration ("HCFA"), ("Chartbook 2000"), p. 6.

592 Chartbook 2000, p. 6. The federal government's contribution to funding (known as the federal matching assistance percentage ("FMAP")) depends on the average per capita income in a state and on compliance with federal policies.

593 Chartbook 2000, p. 9.

594 By 1990, all state Medicaid agencies provided coverage for prescription drugs (National Pharmaceutical Council ("NPC"), *Pharmaceutical Benefits Under State Medical Assistance Programs*, 1991, "Vendor Payments for Prescribed Drugs (1985-1990), pp. 93-94).

595 There are several drug classes that state Medicaid agencies need not cover, including drugs used for anorexia, weight loss, or weight gain; fertility drugs and drugs for the treatment of sexual dysfunction; drugs used for cosmetic purposes or hair growth; drugs used for the symptomatic relief of cough and colds; drugs used to promote smoking cessation; prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations; and nonprescription drugs (Social Security Act, §1927(d)).

596 OBRA 90, Sec 4401(a)(2). States are allowed to subject any covered outpatient drug to prior authorization, as long as the state would provide for dispensing a 72-hour supply in "emergency situations" and would respond to a request for prior authorization within 24 hours of its receipt (OBRA 90, Sec 4401(a)(3), at Sec 1927(d)(5)).

597 60 Fed. Reg. 48442 (September 19, 1995), at 48444.

included in the formulary and there is a written explanation (available to the public) of the basis for the exclusion" and that the drug be available subject to prior authorization.[598] Accordingly, states (including Ohio) generate preferred drug lists ("PDLs") to encourage physicians to prescribe more cost-effective, therapeutically appropriate drugs[599] and use PDLs as a tool in their negotiations with manufacturers regarding supplemental rebates.[600]

291. Through this process, Ohio Medicaid, similar to other TPPs, observes the details of the prescription claim being submitted and has the opportunity to approve or reject claims for reimbursement. Accordingly, for opioid prescription claims submitted to and paid by Ohio Medicaid, it is apparent that the agency affirmatively chose to reimburse the opioid prescription claims as being consistent with the goals of the Medicaid program.

292. The Office of Inspector General ("OIG") of the Department of Health and Human Services examined opioid prescription claims reimbursed by Ohio Medicaid between June 2016 and May 2017 "to identify beneficiaries at serious risk of opioid misuse or overdose and prescribers who ordered opioids for these beneficiaries at higher rates than their peers."[601] Noting that "States … play an important role in ensuring that beneficiaries receive appropriate amounts of opioids", the OIG remarked on the measures taken by Ohio to limit opioid abuse, including more restrictive prescribing guidelines and enhanced requirements for checking the PDMP.[602] The OIG nonetheless concluded that 4,754 non-cancer beneficiaries received "high" amounts of opioids (defined as 120 MME per day for at least three months); over 700 beneficiaries were at serious risk of misuse or

---

598 Social Security Act, Sec 1927(d)(4).

599 OIG Oct 2003, p. 19.

600 See Gencarelli, Dawn, "Medicaid Prescription Drug Coverage: State Efforts to Control Costs," *National Health Policy Forum*, No. 790, May 10, 2003, p. 6: "Given the importance to manufacturers of having their drugs available without prior authorization, states have found that their PDLs can serve as leverage in securing supplemental rebates from manufacturers."

601 OIG, "Opioids in Ohio Medicaid: Review of Extreme Use and Prescribing," July 2018 ("OIG 2018"), pp. 2-3.

602 OIG 2018, pp. 13, 19-20.

overdose; and 481 beneficiaries "received extreme amounts of opioids", with average daily MME of over 240 mg for the entire period.[603]

293. I have examined the data produced by Ohio Medicaid in this case to assess the extent of high levels of opioid prescribing reimbursed by Ohio Medicaid for beneficiaries based in, or receiving treatment in the Counties. For each year from 2010 through October 2018, for those aged older than 15, without a cancer diagnosis and prescribed opioids, I have calculated the average daily MME prescribed to these beneficiaries and the total days of supply associated with those prescriptions. Exhibit VIII-11 shows the number of beneficiaries in each category: days of supply on the horizontal axis (in 30-day increments) and average daily MME on the vertical axis (in 500 MME increments). Numerous individuals received high daily MME levels throughout a given year. The same data, restricted to 2017 and presented in table form in Exhibit VIII-12, shows that 637 patients were prescribed average daily MME in excess of the CDC's recommended 120 MME and 10,870 patients received total days of supply in excess of 90. I note that 483 patients exceeded both of these thresholds, i.e., daily MME in excess of 120 MME for a period of greater than 90 days in the calendar year.

294. Consequently, it is apparent that various causal factors relating to the reimbursement choices made by Ohio Medicaid were relevant in determining the extent of any resulting harms. These factors would have been operational even if Distributors had reported and/or blocked a greater number of "suspicious" orders.

IX. RESPONSE TO OPPOSING EXPERT REPORTS

A. Gruber Report

295. The Gruber Report purports to address whether "to a reasonable degree of certainty in the field of economics, the defendants' shipments of prescription opioids contributed, in whole or part, to the growth in the misuse of opioids and

[603] OIG 2018, pp. 5-7.

the increases in licit and illicit opioid-related mortality over the past 20 years."[604] The Gruber Report reaches the following conclusions: (1) "There is a direct, causal relationship between defendants' shipments of prescription opioids and the misuse and mortality from prescription opioids"; (2) "There is a direct, causal relationship between defendants' shipments of prescription opioids and the misuse of and mortality from illicit opioids, including heroin and fentanyl"; and (3) "The significant increases in all-opioid mortality (i.e., mortality from both prescription and illicit opioids) are largely unrelated to trends in non-opioid drug overdoses, changes in population demographics, or local economic conditions."[605]

296. I understand that the Murphy Report is responding to certain claims made by the Gruber Report with respect to the data analyses in support of these conclusions. Accordingly, my comments address certain areas of overlap between the Gruber Report's claims and the affirmative opinions of my report.

(a) Alleged Relationship between Shipments and Prescription Opioid Misuse and Mortality

297. In addressing the purported causal relationship between shipments of prescription opioids, the misuse of prescription opioids, and prescription opioid-related mortality, the Gruber Report compares the distribution of opioid shipments per capita into "large" counties in 1997 and 2010 and documents a broader variation in 2010 than in 1997.[606] The Gruber Report then claims: "The extreme variation in per capita shipments across areas suggests that prescription activity, which drives shipments to an area, bears little relationship to medical need."[607] The apparent basis for this claim is an analysis allegedly showing that "differences in the demographic and economic characteristics of counties explain very little of the observed differences in per capita shipments."[608] The Gruber Report concludes on this point: "the wide variation in daily per capita MMEs across

604 Gruber Report, ¶ 15.
605 Gruber Report, ¶ 16.
606 Gruber Report, Figure I.14, ¶ 73.
607 Gruber Report, ¶ 74.
608 Gruber Report, ¶ 74.

counties after controlling for differences in demographic and economic characteristics indicates that many shipments were excessive and unnecessary."[609]

298. In acknowledging that it is prescription activity that "drives shipments to an area," the Gruber Report recognizes that Distributors do not themselves choose the level of shipments. Instead, shipments are a response to demand in the form of orders placed by pharmacies, which are in turn a function of the prescriptions filled by those pharmacies. The Gruber Report does nothing to establish that the orders (or some material fraction of these orders) are fraudulent or otherwise illegitimate. It is not apparent that the Gruber Report could do so; for example, as noted earlier in this report, in each year between 1997 and 2017, between 2.5 and 10 percent of dosage units prescribed in Cuyahoga County, and between 0.1 and 4 percent of dosage units prescribed in Summit County, may have been affected by HCPs subsequently disciplined.[610] Similarly, at most 1.8 percent of dosage units in the Counties may have been at issue in circumstances involving doctor shopping while at most 1.3 percent of dosage units in the Counties may have been at issue in circumstances involving pharmacy shopping.[611]

299. Accordingly, it is apparent that the shipments identified by the Gruber Report predominantly resulted from legitimate prescriptions written for legitimate patients. Further, the Gruber Report does not provide adequate support for the extent of overprescribing at the national or county levels, to the extent that this may be an explanation for the observed level of orders. For example, between 2006 and 2010 the DEA's APQ for oxycodone and hydrocodone increased by 83 and 31 percent, respectively;[612] accordingly, increased shipments would be expected. Prescribing trends at the county level can also be expected to depend on incidence rates for conditions typically associated with opioid treatment. For

609 Gruber Report, ¶ 77.

610 See Exhibits VI-19 and VI-20.

611 See Exhibits VI-17 and VI-18.

612 See Exhibits III-6 and III-7.

example, the 2015 incidence rates for cancer and for arthritis are higher in the Counties than the national average.[613]

300. For these reasons, it is misleading to conclude on the basis of a comparison of per capita shipments across counties in 1997 and 2010 that prescription activity bears little relationship to medical need. An increase in shipments and in variation across counties in 2010 would be expected if medical practitioners were making broader use of opioids across a wider variety of conditions and if the incidence of those conditions varied across counties. Further, although the Gruber Report claims to adjust for "differences in pain management needs" across counties,[614] the regression model on which the adjustment is based includes no controls for the county-level incidence of diseases such as cancer and arthritis for which opioid use could be expected, nor does it account for mental health factors that could be expected to be related to drug use.[615] Consequently, the Gruber Report's model of "adjusted" per capita shipments does not account for important characteristics associated with pain management needs and addiction.

301. Finally, even if pharmacy orders underlying the shipments observed in the Gruber Report's analysis were driven in part by overprescribing, the Gruber Report provides no basis to conclude that Distributors caused "excessive and unnecessary" shipments by failing in their duty to monitor for "suspicious" orders. As discussed above, I am not aware that Distributors have a regulatory obligation to monitor orders for influence by possible overprescribing. I am also not aware that Distributors would have the information available to do so.

---

613 "State Cancer Profiles: Incidence Rate Report for Ohio by County, 2011-2015," CDC, https://statecancerprofiles.cancer.gov/incidencerates/index.php?stateFIPS=39&cancer=001&race=00&sex=0&age=001&type=incd&sortVariableName=rate&sortOrder=default#results; "Arthritis National Statistics," CDC, https://www.cdc.gov/arthritis/data_statistics/national-statistics html; "Arthritis State Statistics: Prevalence by County," CDC, https://www.cdc.gov/arthritis/data_statistics/state-data-current htm#county.

614 Gruber Report, ¶¶ 74-75.

615 Gruber Report, Appendix I.D.

(b) Alleged Relationship between Shipments and Illicit Opioid Mortality

302. The Gruber Report contends that although "rising illicit opioid use coincided with declining shipments of prescription opioids and related events around 2010", "changes in illicit mortality generally grew more in areas that received higher shipments."[616] As support, the Gruber Report presents a figure contrasting the average highest quartile counties for shipments with the average lowest quartile for shipments, purportedly showing that "mortality related to heroin and fentanyl moved roughly in parallel in high and low shipment areas prior to 2010, but that mortality from heroin/fentanyl accelerated more in the high shipment counties after 2010."[617]

303. To explain how increased illicit mortality is linked to shipments despite shipments declining over this period, the Gruber Report cites literature allegedly establishing that "prescription opioids have become the predominant gateway to heroin use, a pattern not observed in earlier decades, and thus that the illicit opioid crisis is a direct result of defendants' misconduct."[618] It is further claimed that the "enormous increase in prescription opioid shipments resulting from defendants' misconduct … effectively created a stock of individuals susceptible to illicit opioid use and abuse."[619]

304. The Gruber Report's analysis does not address Cuyahoga or Summit Counties specifically; it does not identify the two Counties in the quartiles, nor does it show that the results hold for counties in the second or third quartiles generally, let alone with respect to the Counties specifically. In addition, the Gruber Report does not explain why Cuyahoga County, which had lower shipments than the

616 Gruber Report, ¶ 85.
617 Gruber Report, ¶ 85, Figure I.18.
618 Gruber Report, ¶ 89.
619 Gruber Report, ¶ 16.

national average, and Summit County, which had higher shipments than the national average,[620] nonetheless had similar opioid mortality levels.

305. Further, the Gruber Report provides no independent empirical basis to support the claim that the trend in illicit opioid mortality post-2010 was caused by the formation of a "stock of individuals" generated prior to 2010 as a result of "excessive and unnecessary" shipments.[621] For example, there is no attempt to quantify the size of this "stock" of individuals in the Counties as of 2010 and compare that number to the number of individuals who suffered heroin or fentanyl overdoses post-2010.

(a) The Gruber Report cites to a study finding that 75 percent of heroin users who began using heroin in the 2000s were introduced to opioids through prescription drugs.[622] This result implies that 25 percent of such heroin users came to heroin via other routes; these individuals would not have been included in any ostensible "stock".

(b) As noted earlier in this report, recent data indicates that approximately 32 percent of those initiating heroin use in 2015 were first-time opioid users, i.e., they had not used any opioid prior to initiating heroin.[623] These individuals would not, by definition, have been included in any ostensible "stock".

(c) Also as noted earlier in this report, the demographics of prescription opioid users differ from the demographics of those who suffer illicit opioid mortality.[624]

620 Gruber Report, Figure I.10.

621 Keyes Report, Section B.7, makes similar claims and is subject to similar criticisms.

622 Gruber Report, ¶ 51, citing Cicero, Theodore et al., "The Changing Face of Heroin Use in the United States," *JAMA Psychiatry*, 71:7, 2014, p. 821.

623 Cicero et al. 2018, p. 267.

624 See, for example, Exhibits VIII-6 and VIII-7.

306. Moreover, in describing the factors that gave rise to the alleged substitution of prescription opioids for heroin, the Gruber Report points to several major events, including "increased enforcement actions by DEA and DOJ, criminal actions and litigation, the growth of state PDMP laws, and increased awareness of addiction risks associated with prescription opioids," along with Purdue's introduction of the ADF reformulation of OxyContin.[625] The Gruber Report claims that "all of these factors contributed to decline in prescription opioid shipments."[626] Under the Gruber Report's own theory then, it would appear that the result of this would be increased illicit opioid uptake.

307. This claim relating to these other factors, however, is inconsistent with the statement that Distributors' shipments had a "direct, causal relationship" with heroin and fentanyl mortality in the post-2010 period. According to the Gruber Report's logic, but for the various factors that led prescription opioid shipments to decrease, mortality from illicit opioids would necessarily have been lower; thus, conduct by Distributors cannot be the sole cause of increased mortality. Even if one were to assume that the Gruber Report is correct in stating that "the illicit opioid crisis that started in 2010 is the direct consequence of the defendants' shipments of prescription opioids in prior years",[627] the Gruber Report's own analysis affirms that illicit opioid mortality is likewise a "direct consequence" of various other factors outside the control of Distributors. In fact, as discussed earlier in this report, the low price and significant profit opportunities associated with illicit fentanyl and its analogues, including carfentanil, coupled with the greater potency of fentanyl and its analogues dictate significant breaks in Plaintiff's theory regarding the causal chain between shipments of prescription opioids and the damages and deaths due to less expensive but more powerful illicit opioids.

625 Gruber Report, ¶ 46.
626 Gruber Report, ¶ 47.
627 Gruber Report, ¶ 99.

308. In discussing fentanyl, the Gruber Report notes that fentanyl's potency gives rise to high overdose risks;[628] it is generally not preferred by drug users, so its emergence is not driven by consumer demand;[629] and its low cost supports high profit opportunities for drug dealers.[630] None of these factors supports the conduct of Distributors as a direct cause of fentanyl-related mortality; on the contrary, all of these factors would tend to suggest that fentanyl-related overdose risks would have been present even if Distributors had reported and/or not shipped a greater volume of "suspicious" orders of prescription opioids. Further, the increase in opioid-related mortality at a time when rates of opioid misuse were flat or declining,[631] has been tied to the greater lethality of fentanyl.[632]

(c) Alleged Lack of Relationship with Economic Conditions

309. The Gruber Report selectively cites to the economic literature in support of the claim that trends in opioid mortality are largely unrelated to economic conditions.[633] This discussion chiefly relies on results from a paper by Christopher Ruhm, which attempts to capture the effects of economic conditions using measures of the changes from 1999 to 2015 in the poverty rate, median household income, median home price, unemployment rate, and import exposure.[634] Additionally, the Gruber Report shows trends in opioid-related mortality for the top and bottom quartiles of "large" counties in terms of their employment to population ratio, suggesting that "the increase in opioid-related mortality cannot simply be attributed to differences in economic opportunity between counties."[635]

---

628 Gruber Report, ¶ 55.

629 Gruber Report, ¶ 61.

630 Gruber Report, ¶ 59.

631 See Exhibit VIII-2 for rates of opioid misuse and abuse and Exhibits VIII-6 and VIII-7 for opioid-related mortality.

632 Singer et al. 2019, pp. 618-619.

633 Gruber Report, ¶¶ 100-103.

634 Ruhm, Christopher J., "Deaths of Despair or Drug Problems?," Frank Batten School of Leadership & Public Policy, University of Virginia, January 2018, Table 1.

635 Gruber Report, ¶ 104.

310. The Gruber Report's discussion of these issues accordingly focuses on indicators of economic conditions that can be expected to respond to relatively short-term fluctuations in the macroeconomic environment. What this approach misses is the importance of secular, structural changes in economic conditions. For example, as noted above, research has found that deteriorating labor market conditions as measured by the change in an area's manufacturing share of employment have a significant causal effect on opioid prescriptions per capita and opioid mortality rates.[636] This is related to the "deaths of despair" literature which finds that increased rates of death by suicide broadly defined (including drug overdose) can be attributed to "a broad deterioration in the lives of Americans without a college degree who entered adulthood after 1970."[637]

311. The Case and Deaton studies that I discuss earlier in this report corroborate that long-term economic factors significantly affect mortality rates. These economic factors are part of a broader set of measures of deterioration, including:

> [T]he decline in marriage rates, the rise in cohabitation, the rise in out of wedlock births, and of parents living apart from children they barely know[;] the decline in the quality of jobs, the increasing lack of opportunity for people without a BA, as well as changing religious practices[;] the decline of unions[; and] that many less-educated people have lives that are economically and socially inferior to those of their parents.[638]

312. While the Gruber Report acknowledges the findings of the "deaths of despair" literature, it makes no attempt to control for these issues or to reconcile them with the claim that trends in opioid-related mortality are "largely unrelated" to economic factors.[639]

---

636 Charles et al. 2018, Table 5.

637 Case, Anne, and Angus Deaton, "Deaths of Despair Redux: A Response to Christopher Ruhm," January 8, 2018, ("Case and Deaton 2018"), p. 2.

638 Case and Deaton 2018, p. 2.

639 Gruber Report, ¶¶ 103-105.

B. Cutler Report

313. The Cutler Report purports to address "the share of various harms imposed on selected departments in each Bellwether government … that is attributable to defendants' misconduct."[640] It proposes a three-step framework, allegedly calculating: (1) "The percentage of harm that is attributable to opioids"; (2) "The percentage of opioid-related harms that is attributable to shipments of prescription opioids";[641] and (3) "The percentage of shipment-related harms that is attributable to defendants' misconduct."[642]

314. I understand that other Defendant reports, including the Murphy Report, respond to claims made in the Cutler Report. Accordingly, my comments address certain areas of overlap between the Cutler Report's claims and the affirmative opinions of my report.

(a) Harms Allegedly Attributable to Opioids

315. In the first step of the analysis, the Cutler Report identifies certain categories of harms and attempts to estimate the percent of harms due to opioid use.[643] The harms that are identified include criminal activity, addiction and mental health activity, the provision of services to children and families, juvenile court activity,

640 Cutler Report, ¶ 9.

641 The Cutler Report does not include a calculation of the percentage of opioid-related harms that is attributable to shipments of prescription opioids. For these calculations the Cutler Report purports to rely on information and analyses in other expert reports, including the Expert Report of Meredith Rosenthal, Ph.D., dated March 25, 2019, and, according to Professor Cutler's deposition testimony, from counsel and/or the McCann Report (Cutler Report, ¶ 9, fn. 7-8; Appendix III.J, ¶ 6 and Table J.1; Cutler Deposition Day 1, pp. 58, 77; Cutler Deposition Day 2, p. 594.) Although Professor Cutler testified that he relied on figures from the McCann Report to create Table J.1 of Appendix III.J (Cutler Deposition Day 2, p. 594), I have not located those figures in any report submitted by Dr. McCann. Further, Dr. McCann's deposition was not completed in time to be considered for the purposes of this report. For these reasons, I reserve the right to change or amend the opinions in this report as appropriate based on any additional information I receive regarding Dr. McCann's opinions and their use in the Cutler Report.

642 Cutler Report, ¶ 21.

643 Cutler Report, ¶ 33.

and medical examiner activity.[644] As my comments are general in nature, I focus on criminal activity as an example.

316. The Cutler Report's analysis is premised on an assumption that in a world in which opioids were not present, or were instead present in some reduced amount, crimes estimated to involve opioid use would have been correspondingly lower.[645] The existence of crime involving opioid use, however, does not imply that crime rates would decline in the absence of opioid use. After all, as discussed earlier in this report, the prevalence of substance abuse and the tie between substance abuse and crime predates the rise of prescription opioids. Further, as shown on Exhibits VIII-3 and VIII-9, those who misuse prescription opioids and/or use non-prescription opioids are more likely to have used an illicit substance in the past. As such, it is not apparent that in the absence of opioids, individuals would not continue to fall victim to substance abuse leading to associated crime.

317. The fact that substance abuse is historically present in some form suggests that many of the individuals who misused opioids likely would have misused an alternative substance had opioids been unavailable. Furthermore, the fact that opioid misusers have characteristics that are correlated with substance abuse in general, suggests that opioid misusers have characteristics that predispose them to misuse or abuse other substances. Taken together, the above analyses indicate a high likelihood that many opioid misusers would have gone on to misuse a different substance had opioids been unavailable. To the extent these individuals were committing crimes motivated by opioid use, as the Cutler Report suggests, it

644 Cutler Report, ¶ 20.

645 I note that at his deposition, Professor Cutler contended that his "Supporting Analysis of Impact of Shipments on Crime" (Cutler Report, Section VIII) neutralizes this critique (Cutler Deposition Day 1, pp. 152-155.) As discussed above, however, shipments respond to prescribing levels; there is no basis to assume shipments are predominantly fraudulent or otherwise illegitimate. As such, the Cutler Report's "supporting" analysis of crime does not demonstrate a causal link between "excessive" shipments and crime. Moreover, the Cutler Report admittedly contains no similar "supporting" analyses for the other categories of harms identified (Cutler Deposition Day 1, pp. 156-161).

is not apparent that the same crimes would not have been motivated by another substance had opioids been unavailable.

(b) Alleged Relationship between Shipments and Opioid-Related Mortality

318. In addressing the share of opioid-related harms that are attributable to shipments of prescription opioids, the Cutler Report uses opioid-related mortality as an indicator of opioid-related harms, stating: "Data on opioid-related mortality provide the most comprehensive information available for identifying the impact of shipments on harms".[646] The Cutler Report proposes two regression frameworks to attempt to estimate the impact of shipments of prescription opioids on opioid-related mortality. The first, termed the "direct approach", seeks to estimate the relationship between changes in county-level opioid-related mortality and the average level of per-capita shipments to the county through 2010, controlling for certain economic and demographic characteristics of the county.[647] The second, termed the "indirect approach", estimates the relationship between opioid-related mortality and economic and demographic characteristics in a period preceding the alleged misconduct; then this model is used to predict the opioid-related mortality rates that would have been expected given the economic and demographic factors present in the period of the alleged misconduct.[648] In my opinion, there are several conceptual problems with these approaches.

319. First, as discussed above, it would appear that legitimate prescriptions drove the pharmacy orders that drove the shipments of prescription opioids. As such, the relationship posited by the Cutler Report between shipments and opioid-related mortality would appear to link directly legitimate prescribing behavior with opioid-related mortality.

646 Cutler Report, ¶ 47.
647 Cutler Report, ¶¶ 66-67.
648 Cutler Report, ¶ 76.

320. Second, opioid-related mortality is, at best, only an imperfect indicator of relevant opioid-related harms. For example, opioid-related mortality rates in the post-2013 period encompass mortality driven by the greater lethality of illicit fentanyl, a drug that is: (i) not generally valued or demanded; (ii) incorporated in the Ohio heroin supply as a result of the prevalence of white powdered heroin in Ohio; and (iii) available in large part due to the low cost of supply and high profit opportunities available to drug dealers.[649] None of these factors suggest that the opioid-related mortality rate is an appropriate proxy for any harms allegedly caused by the activities of Distributors. In fact, it is these characteristics of fentanyl and its analogues, particularly carfentanil, that generate obvious breaks in Plaintiffs' causal chain theory from shipments of prescription opioids to damages and death associated with illicit opioids.

321. Third, the results of the direct regression analysis are misleading with respect to the role and obligations of Distributors in monitoring for "suspicious" orders. This analysis attempts to identify the effect of opioid shipments on changes in opioid-related mortality through 2010, controlling for economic and demographic factors. It finds that, holding other factors constant, "each unit increase in shipments between 1997 and 2010 (measured in MME per capita per day) raises the mortality rate by 4.39 deaths per 100,000, an increase of more than 160 percent over the average rate in the base period."[650] It is implicitly assumed that this result indicates that increased shipments by Distributors caused the increased mortality rate, holding other factors constant.

322. Yet, as discussed earlier in this report, individual Distributors were not in a position to determine or react to aggregate shipment levels. Unlike the DEA, individual Distributors did not have knowledge of total shipments into the County. Further, as discussed above, shipments are driven by demand "pull" forces that originate in prescribing and are transmitted through pharmacy orders. Distributors are not required to (and cannot) monitor or second-guess the

649 See, for example, Gruber Report, ¶¶ 53-54, 58-62.

650 Cutler Report, ¶ 92.

prescribing decisions made by HCPs in contact with their patients. Accordingly, it is not apparent that the Cutler Report's direct approach results in a model that permits a reliable evaluation of the effects of conduct by Distributors.

323. Fourth, the results of the indirect model are likewise misleading with respect to the role and obligations of Distributors. The Cutler Report employs two variants of the indirect model. A first version attempts to explain variation across counties in the average death rate due to illicit opioids from 2008 to 2010, controlling for county-specific economic and demographic factors.[651] The results are then used to predict "but for" mortality rates for illicit opioids from 2011 to 2016 "that would have been observed in the absence of the shift into illicit opioids after 2010 that resulted from earlier shipments of prescription opioids."[652] A second version of the model is estimated to relate the county-specific average total opioid-related mortality rate from 1993 to 1995 to economic and demographic factors, with the estimated model then used to predict opioid-related mortality rates for the post-1995 period.[653] For both versions, the residual calculated by subtracting "but for" mortality from actual mortality is used to construct a measure of the harms attributable to Defendants.[654]

324. This analysis thus embeds a strong form of the "gateway" assumption addressed above, such that differences between post-2010 opioid-related mortality and the levels that would have been predicted based on earlier years are implicitly attributed, in part, to individuals shifting from misuse of prescription opioids to illicit opioid use.[655] As discussed earlier in this report, however, such transitions are atypical. Prescription opioid misusers that go on to use illicit opioids also have characteristics that are associated with a predisposition to substance abuse, implying a likelihood of some level of substance abuse in the post-2010 period

651 Cutler Report, ¶ 94.
652 Cutler Report, ¶ 97.
653 Cutler Report, ¶¶ 98, 100.
654 Cutler Report, ¶¶ 97, 100.
655 Cutler Report, ¶¶ 112, 116.

given the ready availability of illicit opioids during that period.[656] The indirect model's attribution of residual harms in the post-2010 period to Defendants is likewise misplaced given the acknowledgement that "restrictive policies" outside the control of Distributors "contributed to increased use of illicit opioids and further harms".[657] In addition, the Cutler Report fails to account for the change in the presence of fentanyl and its analogues, including carfentanil, in the post-2010 period as compared to the earlier periods.

C. McCann Report

325. The McCann Report states the following as its mandate: (i) "to document how I processed, validated and augmented opioid transaction data produced by the … DEA … and from the Defendants"; (ii) "to summarize shipments in the ARCOS Data"; and (iii) "to report the results of applying certain algorithms to the ARCOS Data."[658] I understand that other Defendant expert reports discuss issues considered in the McCann Report. The discussion below focuses on the third issue, the McCann Report's application of "certain algorithms".

(a) Analyses Allegedly Identifying Suspicious Orders

326. The McCann Report undertakes a series of analyses said "to identify transactions meeting specified criteria."[659] The McCann Report characterizes these analyses as a "non-exhaustive set of algorithms that can be systematically applied to the ARCOS data"[660] in order to estimate alleged Distributor misconduct by purporting to identify allegedly "suspicious" orders that should have been reported or not shipped. Estimates ostensibly derived from the McCann Report's

---

656 For example, as noted above, according to studies, a material fraction of heroin users did not misuse prescription opioids prior to initiating heroin (Cicero et al. 2018, p. 267).

657 Cutler Report, ¶ 18 and Figure III.1. Note that the Cutler Report (fn. 53) admits the problems posed by this approach, stating: "The indirect regression attributes the entirety of the unexplained opioid-related mortality to shipments. To the extent that other factors not modelled in the 'baseline' regression contributed to increases in opioid mortality, the indirect approach has the potential to overstate the impact of defendants' actions."

658 McCann Report, ¶¶ 10-12.

659 McCann Report, ¶ 130.

660 McCann Report, ¶ 21.

analysis are represented in the Cutler Report as the fraction of opioid shipments resulting from Distributor misconduct.[661] The McCann Report bases its conclusions on assumptions that result in an overstated estimate of Distributor misconduct.

327. The McCann Report defines the "Maximum Monthly, Trailing Six-month Threshold" as identifying "transactions that cause the number of dosage units shipped by a Distributor to a Pharmacy in a calendar month to exceed the highest number of dosage units shipped by the Distributor to the Pharmacy in any one of the six preceding calendar months."[662] This approach does not take into account legitimate reasons why a pharmacy's order in a given month would exceed the monthly order in any of the previous six months.

(a) For example, as discussed earlier in this report, the DEA increased its APQ of oxycodone, hydrocodone, and other opioids. In total, between 2006 and 2010, the DEA's APQ increased by 83 and 31 percent for oxycodone and hydrocodone respectively. As the DEA's quota is intended to reflect expected demand, an increase would be expected to be followed by an increase in the prescribing and thus the ordering of opioids.

(b) Further, newly opened pharmacies would take time to attract new customers and would thus be expected to increase their shipments over time.

(c) As discussed earlier in this report, during the period from 2006 to 2014, new opioid products were introduced and existing products were reformulated as ADFs. The introduction of these products and the initial stocking of these products may be expected to lead to an increase in orders by pharmacies.

661 Cutler Deposition Day 1, pp. 80-81.

662 McCann Report, ¶ 131.

(d) In addition, a pharmacy may experience an influx of patients if, for example, new businesses, new doctors' offices or a new hospital opened up nearby, thereby increasing the number of nearby patients being prescribed an opioid.

328. Additional threshold analyses performed in the McCann Report include "Twice Trailing Twelve-Month Average Pharmacy Dosage Units";[663] "Three Times Trailing Twelve-Month Average Pharmacy Dosage Units";[664] "Maximum 8,000 Dosage Units Monthly";[665] and "Maximum Daily Dosage Units".[666] As above, these methodologies do not take into account the preceding legitimate reasons why a pharmacy's order in a given month would exceed these arbitrary thresholds. Further, particularly with respect to the "Maximum 8,000 Dosage Units Monthly" threshold, I note as discussed earlier in the report, there is considerable variation in the average monthly ordering across counties and pharmacies.[667] Factors expected to affect a pharmacy's order size include population and economic activity in the surrounding area, proximity to hospitals or prescriber concentrations, and sales of non-controlled substances.

329. To the extent that any such thresholds are informative, a more appropriate interpretation is that while such thresholds may flag some "suspicious" orders, they may also incorrectly flag legitimate orders. The McCann Report appears to concede this concern, stating: "The purpose of identifying transactions – to

---

663 According to the McCann Report (¶ 136), this threshold identifies "transactions that cause the number of dosage units shipped by a Distributor to a Pharmacy in a calendar month to exceed twice the trailing twelve-month average dosage units to retail and chain pharmacies served by the Distributor."

664 According to the McCann Report (¶ 140), this threshold identifies "transactions that cause the number of dosage units shipped by a Distributor to a Pharmacy in a calendar month to exceed three times the trailing twelve-month average dosage units to retail and chain pharmacies served by the Distributor."

665 According to the McCann Report (¶ 144), this threshold identifies "transactions that cause the number of dosage units shipped by a Distributor to a Pharmacy in a calendar month to exceed 8,000 dosage units."

666 According to the McCann Report (¶ 148), this threshold identifies "transactions that cause the number of dosage units shipped by a Distributor to a Pharmacy in a day to exceed a number of dosage … units that varies by drug type and within some drug types by formulation."

667 See Exhibits VI-4 to VI-9.

determine which transactions warrant some further due diligence – is likely to only be met by flagging more transactions than those which are used to fill medically unnecessary prescriptions."[668] It is reasonable to expect that most (based upon the issues raised earlier in this report) of the flagged orders would, upon due diligence by individual Distributors, be deemed legitimate. Yet the McCann Report does not allow for this likelihood and instead assumes the opposite, apparently without support: that upon due diligence all of the flagged orders would have been deemed illegitimate and blocked.

330. A further assumption renders these biased estimates of "suspicious" orders even less informative for the purposes to which they are apparently intended. For each threshold, the McCann Report assumes at the instruction of counsel "that the Distributor did not effectively investigate the flagged transactions and so every subsequent transaction of that drug code is also flagged because the Distributor had an unfulfilled obligation to detect and investigate the first flagged transaction."[669]

331. This assumption makes no sense. It is not apparent that a shipped order implies a lack of due diligence. Further, based upon the issues raised earlier in this report, it is likely that the majority of these orders would have been deemed legitimate by an individual Distributor. As a result, it is reasonable to expect that most flagged orders would, upon due diligence, be deemed legitimate and ultimately shipped. In addition, the fact that these pharmacies continued to place orders suggests that the orders being placed were legitimate. If these pharmacies were consistently placing orders for diversionary purposes, they must have consistently evaded detection by the very parties actually in possession of the information that could be used to determine diversion: the DEA and the Ohio BOP.

668 McCann Report, ¶ 160.

669 McCann Report, ¶¶ 132, 136, 140, 144, 148.

332. Solely by virtue of this Plaintiffs' counsel instruction, the number of "suspicious" orders in Cuyahoga County identified in the McCann Report increased by:

(a) 1,271,618 orders (76 percent) according to the Maximum Monthly, Trailing Six-month Threshold;[670]

(b) 763,723 orders (46 percent) according to the Twice Trailing Twelve-Month Average Pharmacy Dosage Units threshold;[671]

(c) 434,698 orders (26 percent) according to the Three Times Trailing Twelve-Month Average Pharmacy Dosage Units threshold; [672]

(d) 713,969 orders (43 percent) according to the Maximum 8,000 Dosage Units Monthly threshold;[673] and

(e) 1,225,867 orders (83 percent) according to the Maximum Daily Dosage Units threshold.[674]

333. With respect to Summit County, the number of "suspicious" orders identified in the McCann Report increased by:

(a) 811,825 orders (75 percent) according to the Maximum Monthly, Trailing Six-month Threshold;[675]

(b) 676,478 orders (63 percent) according to the Twice Trailing Twelve-Month Average Pharmacy Dosage Units threshold;[676]

670 McCann Report, ¶ 133 and Table 24.
671 McCann Report, ¶ 137 and Table 26.
672 McCann Report, ¶ 141 and Table 28.
673 McCann Report, ¶ 145 and Table 30.
674 McCann Report, ¶ 149 and Table 32.
675 McCann Report, ¶ 134 and Table 25.
676 McCann Report, ¶ 138 and Table 27.

(c) 436,234 orders (41 percent) according to the Three Times Trailing Twelve-Month Average Pharmacy Dosage Units threshold; [677]

(d) 563,914 orders (52 percent) according to the Maximum 8,000 Dosage Units Monthly threshold;[678] and

(e) 804,324 orders (87 percent) according to the Maximum Daily Dosage Units threshold.[679]

334. The end result of the McCann Report's threshold analyses is that up to 83 percent of shipments to Cuyahoga and Summit Counties in a year should have been not shipped or reported as "suspicious".[680] The McCann Report, however, fails to consider the impact of such a draconian result on the legitimate prescriptions for opioids that would not have been dispensed. A reasonable goal of not shipping and reporting "suspicious" orders is to minimize diversion, presumably subject to fulfilling the legitimate medical needs of patients.

(b) Analyses Allegedly Identifying Excessive Shipments

335. The McCann Report purports to calculate an "upper bound on the medically necessary opioid MME per capita" by assuming "that all prescriptions of opioids in 1997 and in 2018 were medically necessary",[681] and a "lower bound" on the medically necessary opioid MME per capita by assuming "that all prescriptions of opioids in 1997 were necessary and opioid use per capita beyond 1997 levels were unnecessary."[682] The difference between actual shipments "and the baseline

677 McCann Report, ¶ 142 and Table 29.

678 McCann Report, ¶ 146 and Table 31.

679 McCann Report, ¶ 150 and Table 33.

680 Supplemental Expert Report of Craig J. McCann, Ph.D., CFA, April 3, 2019 ("McCann Supplemental Report"), Tables A-E.

681 McCann Report, ¶ 155. The upper bound in a given year is interpolated based on MME shipped per capita in 1997 and 2018.

682 McCann Report, ¶ 156.

is an estimate of the excessive opioids shipped into Ohio."[683] This oversimplified approach results in an unreliable estimate of allegedly excessive shipments.

336. The choice to treat 1997 opioid use per capita as a lower bound for the "baseline" is unsupported. I am not aware of any reason to expect that the 1997 level of prescribing represents legitimate medical needs for 1998 through 2017. As discussed earlier in this report, the post-1997 period is associated with: (i) an increased focus on the effective treatment of pain for patients with legitimate medical needs; (ii) a variety of new FDA-approved products for the treatment of pain; (iii) increases in the DEA's quota for the production of various opioids; and (iv) the expansion of pharmaceutical coverage resulting from Medicare Part D and broader coverage by Ohio Medicaid. All of these are factors that could potentially drive increases in opioid prescribing but that the McCann Report does not consider.

337. The choice to treat interpolated shipments between 1997 and 2018 as an upper bound for the "baseline" is equally unsupported. For example, the decline in utilization in recent years has been associated with changes in guidelines and rules that place more stringent limits on opioid use in pain treatment. As discussed earlier in this report, however, this approach may have resulted in an increase in patient distress due to untreated pain.

338. Additionally, the McCann Report's allegedly excessive shipment analysis is irrelevant to assessing the alleged misconduct on the part of Distributors. As discussed, increased shipments were the result of increased prescribing and enabled by the DEA's increases in APQ. Further, Distributors have no ability to assess whether a prescription was consistent with legitimate medical needs; as discussed above, it is apparent that legitimate prescribing accounts for the vast majority of prescriptions written. As such, the McCann Report's allegedly excessive shipment analysis cannot be useful in any assessment that requires a

683 McCann Report, ¶ 158.

meaningful distinction between shipments resulting from illegal diversion and those resulting from legitimate prescribing.

X. ABATEMENT

339. I understand that Plaintiffs have submitted materials proposing various future efforts to abate opioid-related harms.[684] These materials are apparently in support of Plaintiffs' allegations that the Counties are expecting to bear significant ongoing costs with respect to opioid-related harms and treatment.[685] In some cases, these costs are based on projections for a base of patients requiring treatment that remains constant over time.[686] Attached as Appendix C is a list of the abatement program categories proposed by Plaintiffs' experts.

340. In this section, I begin by considering the issue of potential abatement burdens related to the size of the patient population and whether these burdens are expected to continue at a sustained level or to decline, given information suggesting a peak in indicators of opioid use and/or abuse. Next I consider whether it is sensible for the Counties to expect to incur burden costs in the future given federal programs and interventions already in place. Finally, I summarize data from Ohio Medicaid made available to me on the per-patient cost of a diagnosis of opioid abuse or dependence, or an opioid overdose; as well as the costs that may be associated with a diagnosis of NAS.

A. Introduction

341. There is support for the hypothesis that opioid misuse and overdose deaths either have reached a peak or will reach a peak in the near future, and accordingly that the affected base of individuals would be expected to decline into the future. Nationally, the number of individuals initiating non-medical use of prescription

684 Alexander Report, ¶ 40; Liebman Report, ¶ 3; Keyes Report, p. 3.

685 For example, see Liebman Report, ¶ 18.

686 See Liebman Report, Table C.1.

opioids has declined since 2008, based on NSDUH estimates.[687] In Ohio, both the number of drug overdose deaths involving prescription opioids and the percentage of drug overdose deaths involving prescription opioids have declined since 2011.[688] Further, information compiled by the Counties indicates a potential decline in illicit opioid overdoses in 2018 relative to prior years. For example, the Cuyahoga County Medical Examiner's Office reports a decline in heroin overdose deaths from 320 in 2016 to 153 in 2018; in fentanyl (not including carfentanil) overdose deaths from 492 in 2017 to 404 in 2018; and in carfentanil overdose deaths from 191 in 2017 to 24 in 2018.[689] Summit County Public Health indicates in a brief dated February 2019 that overdose deaths "began a rapid decline" from 310 in 2016 to 105 in 2018; of drugs mentioned on overdose death certificates, heroin declined from 2013 to 2018; fentanyl declined from 2016 to 2018; and carfentanil declined from 2017 to 2018.[690] Based on these indicators, it would appear that a peak has already been reached with respect to the effects of opioid misuse.

342. It is understood that a key driver in the course of a drug abuse "epidemic" is the rate of initiation by new users; when this rate declines, the overall level of abuse and the burden associated with that abuse will eventually follow.[691] Exhibit X-1 shows the national trend in heroin initiation by age group, from 2002 to 2017. It appears that heroin initiation by users aged 12-17 peaked in 2002 and again in 2011; initiation by users aged 18-25 peaked in 2011; and initiation by users aged 26 and older peaked in 2014. Levels in 2017 are statistically significantly lower

687 Chen, Qiushi et al., "Prevention of Prescription Opioid Misuse and Projected Overdose Deaths in the United States," *JAMA Network Open*, 2:2, 2019, Supplement eFigure 5, eTable 1.

688 "2017 Ohio Drug Overdose Data: General Findings," Ohio Department of Health, Figures 1 and 2.

689 "Heroin/Fentanyl/Cocaine Related Deaths in Cuyahoga County," Cuyahoga County Medical Examiner's Office, March 6, 2019, http://medicalexaminer.cuyahogacounty.us/pdf_medicalexaminer/en-US/HeroinFentanylReports/CCMEOFeb2019HeroinFentanylCocaine.pdf, p. 2.

690 "Population Health Vital Statistics Brief: Drug Overdoses, February 1 – February 28, 2019," Summit County Public Health, Population Health Division, https://www.scph.org/sites/default/files/editor/drug%20overdoses%20data%20brief%20february%202019_0.pdf, p. 7.

691 Winkler et al., "Estimating the Relative Efficiency of Various Forms of Prevention at Different Stages of a Drug Epidemic," *Socio-Economic Planning Sciences*, 38, 2004, p. 45, Figure 1.

than peak levels for all age groups. National rates of heroin use have held approximately constant during the past five years.[692] On the basis of these initiation trends it may be expected that overall heroin use (and associated harms) will decline.

B. Plaintiffs' Characterizations of Abatement Programs

343. Plaintiffs' experts have proposed a variety of prevention and treatment programs that they claim would reduce the risk of opioid-related harm and overdose deaths in Cuyahoga and Summit Counties. I have not performed a comprehensive analysis of the Alexander, Keyes, and Liebman Reports, but I have examined some of the material presented in these reports concerning abatement measures.[693] I have three general observations.

344. First, the Keyes Report makes no effort to ascertain the actual needs of either of the Counties for additional financial, institutional, or other resources for delivery of the recommended abatement services. The report does not identify what city, county, state, national, and private resources are already available to residents of each County, whether those resources are adequate, or the extent (if any) to which either County is itself responsible for delivering and/or paying for such services.[694] Without this information, abstract conclusions about "needs" within the geographies of these counties are uninformative.

345. The Keyes Report's "estimates" of the numbers of residents of each of the Counties who suffer from opiate use disorder are not reliable.[695] Instead of using NSDUH data, these estimates are based on a single statistic reported in an article that pooled the results of several epidemiological studies addressing the causes of

---

692 "Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health," SAMHSA, https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report, Figure 22.

693 Keyes Report, Sections C and F; Alexander Report, ¶¶ 40-181; Liebman Report, Sections VI and VII.

694 Keyes Report, Sections C and F.

695 Keyes Report, pp. 32-34. In her deposition, Professor Keyes clarified that the estimates were instead of persons who are dependent on or regular users of opioids (Deposition of Katherine Keyes, April 29, 2019 ("Keyes Deposition"), pp. 389-391).

mortality among dependent and regular drug users.[696] The authors of the article warned that data from the studies reviewed were "heterogeneous" and varied across a number of factors that are material here, including location and time period.[697] Most studies were from outside the U.S.; none focused on Ohio, and all pre-dated 2009. The populations studied also varied. Given these considerations, the use of this single pooled statistic in the Keyes Report cannot be viewed as generating reliable results.

346. Second, the Alexander and Liebman Reports purport to estimate the financial impact of their proposed abatement programs in each of the Counties. Neither estimate, however, is based on any accurately measured demand for opioid-related services, or the extent (if any) to which either County is itself responsible for delivering and/or paying for such services.[698] Further, neither the Alexander nor Liebman Reports link the cost estimates of their proposed abatement programs to the alleged misconduct of Distributors and ultimately do not calculate damages to the Counties.

347. The Alexander Report analyzes the national costs of fifteen abatement programs and uses 2017 opioid overdoses as a proxy for global abatement needs to extrapolate a 10-year estimate of abatement costs for the Counties.[699] I understand, however, that the fifteen national abatement programs considered are run and paid for at the national level. To the extent that this is true, these are not costs being incurred by the Counties. Further, The Alexander Report admits that the goal of this analysis was not to identify precise costs and that "detailed assessments of the specific costs within Cuyahoga and Summit Counties will be required" due to the limitations in extrapolating from national estimates to

---

696 Degenhardt, Louisa, et al., "Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies," *Addiction*, 106:1, 2011 ("Degenhardt, et al. 2011") pp. 32-51 (cited as reference 151 in the Keyes Report).

697 Degenhardt, et al. 2011, pp. 46-47.

698 Alexander Report, ¶ 181 ("My analyses do not address how abatement costs should be shared across different parties."); Liebman Report, ¶ 17 ("My analysis does not address how abatement costs should be shared among various entities or parties.").

699 Alexander Report, ¶¶ 176-180.

specific localities.[700] Accordingly, there is no basis for the Alexander Report to use a 1.5 percent multiplier as an estimate of the portion of the national program costs that would be a burden on the Counties.[701]

348. The reported 15-year cost estimates for abatement programs proposed in the Liebman Report are also not reliable. This report provides an estimated 15-year cost range for each County in order to account for the uncertainty and alterative assumptions about the future treatment needs of opioid users.[702] The failure to address the actual needs of the Counties is apparent given the Liebman Report's admission that the abatement strategy and associated costs will need to be updated based upon the "conditions on the ground" in the Counties.[703]

349. Third, the U.S. government presently offers opioid-related prevention and treatment programs that are analogous to most, if not all, of the abatement programs proposed by Plaintiffs' experts. I am also aware that certain current opioid-related prevention and treatment services offered at the state, county, and city levels are analogous to the Plaintiffs' recommended abatement programs. I understand that those analogous state, county, and city programs are addressed in the expert report of Matthew G. Bialecki, CPA, CFF, CGMA, dated May 10, 2019 ("Bialecki Report"), and therefore, I do not include such programs here. The remainder of this section describes the various prevention and treatment programs offered by the federal government to reduce the risk of opioid-related harm and overdose deaths, and to mitigate their effects.[704]

---

700 Alexander Report, ¶ 180.

701 Alexander Report, ¶ 180.

702 Liebman Report, Tables 1 and 2.

703 Liebman Report, ¶ 85.

704 The prevention and treatment programs described below are not intended to be a complete and comprehensive list of all opioid-related services provided by the federal government. Rather, these programs constitute a sample of the federal programs that are analogous to Plaintiffs' experts' proposed abatement programs (see Appendix C).

C. Overview of Prevention Programs Offered by the Federal Government

350. Abatement programs focused on the prevention of opioid-related harms and overdoses include media campaigns, drug disposal programs, education and training programs, and school-based prevention programs.[705] Each of these is briefly addressed in turn.

(a) Media Campaigns

351. In September 2017, the CDC released the "Rx Awareness" campaign to increase awareness about the risks of prescription opioids and deter inappropriate use.[706] The campaign features accounts of individuals living in recovery, and those who have lost someone to an overdose. The CDC ran digital, radio, and out-of-home campaign ads for 14 weeks in select states, including Ohio, and found that the campaign ads were a powerful and effective way to raise awareness and increase knowledge about the dangers of prescription opioids.[707] The CDC has since launched the campaign in 22 additional Overdose Prevention in States funded states.[708]

352. The "Youth Opioid Prevention Ad Campaign" initiative was announced in June 2018 by the Office of National Drug Control Policy ("ONDCP"), in partnership with the Ad Council and Truth Initiative. This public awareness advertising

---

705 For purposes of this section, I offer no opinions on the efficacy or advisability of the abatement programs discussed herein. Rather, the sole purpose of this section is to provide a general overview of the opioid-related services offered by the federal government that are presently available to the Counties.

706 "CDC launches campaign to help states fight prescription opioid epidemic," CDC Press Release, September 25, 2017, https://www.cdc.gov/media/releases/2017/p0925-rx-awareness-campaigns html.

707 "Campaign Resources," CDC, https://www.cdc.gov/rxawareness/resources/index.html.

708 "Addressing the Prescription Opioid Crisis: CDC Rx Awareness Campaign Overview," CDC, 2017, https://www.cdc.gov/rxawareness/pdf/Overview-Rx-Awareness-Resources.pdf, p. 17; "CDC launches campaign to help states fight prescription opioid epidemic," CDC Press Release, September 25, 2017, https://www.cdc.gov/media/releases/2017/p0925-rx-awareness-campaigns html. See also "Opioid Overdose: State Information," CDC, https://www.cdc.gov/drugoverdose/states/index html.

campaign is focused on preventing and reducing opioid misuse among youth and young adults.[709]

(b) Drug Disposal Programs

353. The DEA began National Prescription Drug Take Back Day in 2010. The DEA hosts events every six months where temporary collection sites are set up in communities nationwide for safe disposal of prescription drugs in partnership with federal, state, local and tribal law enforcement, businesses, medical offices, federal agencies, and first responders.[710]

354. As discussed earlier in this report, another option for the disposal of unneeded medicines is to transfer these medicines to DEA-registered collectors, which safely and securely collect and dispose of pharmaceuticals containing controlled substances and other medicines. Authorized permanent collection sites may be in retail pharmacies, hospital or clinic pharmacies, and law enforcement facilities. Some authorized collection sites may also offer mail-back programs or collection receptacles to assist consumers in safely disposing of their unused medicines.[711]

355. The U.S. government also offers grants to states, local governments, and Indian tribes through the Comprehensive Opioid Abuse Program ("COAP"). These grants are intended to provide services primarily relating to opioid abuse, including prescription drug take-back programs.[712]

---

709 "What is the Opioid Epidemic," Opioids Truth, https://opioids.thetruth.com/o/home; "Statement from the Press Secretary Regarding the Youth Opioid Prevention Ad Campaign," The White House Statements & Releases, June 7, 2018, https://www.whitehouse.gov/briefings-statements/statement-press-secretary-regarding-youth-opioid-prevention-ad-campaign/.

710 "Welcome," Take Back Day, https://takebackday.dea.gov/; "DEA Heads First-ever Nationwide Prescription Drug Take-back Day," The United States Department of Justice Press Release, August 19, 2010, https://www.justice.gov/opa/pr/dea-heads-first-ever-nationwide-prescription-drug-take-back-day.

711 "Disposal of Unused Medicines: What You Should Know," FDA, https://web.archive.org/web/20110709064744/https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/%20ensuringsafeuseofmedicine/safedisposalofmedicines/ucm186187 htm.

712 "Comprehensive Opioid Abuse Program (COAP)," Bureau of Justice Assistance, https://www.bja.gov/ProgramDetails.aspx?Program_ID=72; "Comprehensive Opioid Abuse Site-based Program FY 2019 Competitive Grant Announcement," April 5, 2019, https://www.bja.gov/funding/COAP19.pdf, p. 7.

(c) Education and Training Programs

356. The federal government provides several educational training programs on drug abuse, including "Disposal of Unused Medicines: What You Should Know,"[713] the National Institute on Drug Abuse's Resources for Educators,[714] the National Institute on Drug Abuse for Teens,[715] the National Drug and Alcohol Facts Week,[716] and the American Heart Association's Opioid Education for Non-Clinical Staff and Lay Responders.[717]

357. The "Up and Away and Out of Sight" Partnership is an educational program to emphasize the importance of safe medicine storage. It is an initiative of PROTECT, a collaboration among public health agencies, private sector companies, professional organizations, consumer/patient advocates, and academic experts, in partnership with the CDC. The campaign encourages adults to keep medicine out of reach of small children and to teach children about medicine safety.[718]

358. The HHS Pathways to Safer Opioid Use is an interactive training tool that teaches health care providers how to communicate the safe use of opioids to manage

---

713 "Disposal of Unused Medicines: What You Should Know," FDA, https://web.archive.org/web/20110709064744/https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/%20ensuringsafeuseofmedicine/safedisposalofmedicines/ucm186187 htm.

714 "Parents & Educators," NIH, https://www.drugabuse.gov/parents-educators.

715 "Teens: Drug Use and the Brain," National Institute on Drug Abuse for Teens, https://teens.drugabuse.gov/.

716 "National Drug and Alcohol Facts Week," National Institute on Drug Abuse for Teens, https://teens.drugabuse.gov/national-drug-facts-week.

717 "Opioid Education for Non-Clinical Staff and Lay Responders," American Heart Association, https://elearning.heart.org/course/320?utm_source=google&utm_medium=cpc&utm_term=%2B%20opioid%20%2Beducation&utm_campaign=E-Learning%20|%20Opioid%20Education&gclid=EAIaIQobChMIjfTpydPK4QIVEI3ICh0n1gCZEAMYASAAEgL_W_D_BwEc.

718 "Substance Misuse Prevention Media Campaigns," SAMHSA, https://web.archive.org/web/20181124185432/https://www.samhsa.gov/capt/tools-learning-resources/prevention-media-campaigns; "Put your medicines up and away and out of sight," Up and Away, https://www.upandaway.org/; "PROTECT Initiative: Advancing Children's Medication Safety," CDC, https://www.cdc.gov/MedicationSafety/protect/protect_Initiative.html.

chronic pain. It is based on the opioid-related recommendations in the National Action Plan for Adverse Drug Event Prevention ("ADE Action Plan").[719]

359. In April 2019, the FDA launched a new education campaign to help Americans understand the importance of removing and properly disposing of unused prescription opioids from their homes. The "Remove the Risk" campaign targets women ages 35-64, who are most likely to oversee household health care decisions and often serve as the "gatekeepers" to opioids and other prescription medications in the home. The new initiative is part of the FDA's continued efforts to decrease unnecessary exposure to opioids.[720]

(d) School-Based Prevention Programs

360. The DEA has joined Discovery Education to create comprehensive, no-cost, digital curriculum tools to combat opioid misuse. The "Operation Prevention" materials are available today in every school, home, and state in the nation, with Virtual Field Trips, English & Spanish language standards-aligned K-12 curriculum resources, a parent tool kit, and a national peer-to-peer video challenge.[721]

361. NIDA for Teens: The Science Behind Drug Abuse is a National Institute on Drug Abuse, NIH, and HHS campaign geared toward adolescents ages 11 to 15. NIDA for Teens uses a blog, videos, and drug factsheets to educate youth, parents, and teachers about the science behind drug misuse. The campaign website contains information on a wide array of substances, including emerging drug trends.[722]

---

719 "Pathways to Safer Opioid Use," Health.gov, https://health.gov/hcq/training-pathways.asp.

720 "FDA launches public education campaign to encourage safe removal of unused opioid pain medicines from homes," FDA, April 25, 2019, https://www fda.gov/news-events/press-announcements/fda-launches-public-education-campaign-encourage-safe-removal-unused-opioid-pain-medicines-homes.

721 "Take the Pledge to Prevent Opioid Misuse," Operation Prevention, https://www.operationprevention.com/.

722 "Substance Misuse Prevention Media Campaigns," SAMHSA, https://web.archive.org/web/20181124185432/https://www.samhsa.gov/capt/tools-learning-resources/prevention-media-campaigns.

362. ONDCP also manages the Drug Free Communities Support program, which provides grants to coalitions to implement comprehensive, long-term plans and programs to prevent and treat substance abuse among youth.[723] The fiscal year 2018 funding was $15 million for approximately 120 grant awards for up to five years to community-based coalitions.[724]

D. Overview of Treatment Programs Offered by the Federal Government

363. Abatement programs focused on the treatment of opioid-related harms and overdoses include the investment in the "treatment system," MAT, naloxone administration and distribution, detoxification programs, inpatient and outpatient therapy, recovery housing, and programs for adolescents. Each of these is briefly addressed in turn.

(a) Investment in the "Treatment System"

364. The CDC declared an opioid epidemic in 2011 and the ONDCP released a government wide plan to address the epidemic that same year. While the plan emphasized reducing prescription opioid misuse, successful implementation of the plan was linked to the ACA and Medicaid expansion. CMS finances health care services, including substance abuse treatment services, through Medicare and the federal share of Medicaid. The ACA required coverage for substance use disorder treatment and expanded access to substance use disorder treatment.[725]

365. The CDC also awarded $155.5 million on August 31, 2018, to increase support for states and territories working to prevent opioid-related overdoses, deaths, and other outcomes, $12 million in funds to support 11 Tribal Epidemiology Centers

---

723 "Grants & Programs," The White House, https://www.whitehouse.gov/ondcp/grants-programs/; "Drug-Free Communities (DFC) Support Program," SAMHSA Announcement, December 16, 2015, https://www.samhsa.gov/grants/grant-announcements/sp-16-001.

724 "Drug-Free Communities (DFC) Support Program – New," SAMHSA Announcement, January 12, 2018, https://www.samhsa.gov/grants/grant-announcements/sp-18-002.

725 "Tracking Federal Funding to Combat the Opioid Crisis," Bipartisan Policy Center, https://bipartisanpolicy.org/wp-content/uploads/2019/03/Tracking-Federal-Funding-to-Combat-the-Opioid-Crisis.pdf, p. 9.

and 15 tribal entities, and $27 million to nine non-governmental organizations, which will support states and territories with staffing, procurement, and training to enhance local public health capacity.[726]

366. SAMHSA awarded more than $930 million in State Opioid Response grants in 2018 to support a comprehensive response to the opioid epidemic and expand access to treatment and recovery support services.[727] Ohio was one of the states that received SAMHSA funding through a State Opioid Response grant.[728]

367. The Health Resources and Services Administration ("HRSA") awards funding to combat the opioid crisis. The investments enable HRSA-funded community health centers, academic institutions, and rural organizations to expand access to integrated substance use disorder and mental health services. In 2018, HRSA awarded over $396 million to combat the opioid crisis.[729] Ohio was awarded funding through the Behavioral Health Workforce Education and Training, and Enhancing Behavioral Health Workforce awards; Rural Communities Opioid Response Program-Planning; and Health Center, and Rural Health Opioid Programs, among others.[730]

368. The Comprehensive Addiction and Recovery Act ("CARA") of 2016 authorized COAP for states, units of local government, and Indian tribes. These grants are intended to provide services primarily relating to opioid abuse, including

726 "HHS Awards Over $1 Billion to Combat the Opioid Crisis," HHS Press Release, September 19, 2018, https://www.hhs.gov/about/news/2018/09/19/hhs-awards-over-1-billion-combat-opioid-crisis.html.

727 "HHS Awards Over $1 Billion to Combat the Opioid Crisis," HHS Press Release, September 19, 2018, https://www.hhs.gov/about/news/2018/09/19/hhs-awards-over-1-billion-combat-opioid-crisis.html.

728 "State Opioid Response Grants: Funding Opportunity Announcement (FOA) No. TI-18-015," SAMHSA, https://www.samhsa.gov/sites/default/files/grants/pdf/sorfoafinal.6.14.18.pdf, pp. 80-81.

729 "HHS Awards Over $1 Billion to Combat the Opioid Crisis," HHS Press Release, September 19, 2018, https://www.hhs.gov/about/news/2018/09/19/hhs-awards-over-1-billion-combat-opioid-crisis.html.

730 "Search HRSA awarded Grants," https://data.hrsa.gov/tools/find-grants.

treatment.[731] CARA also led to the creation of the Pain Management Best Practices Inter-Agency Task Force, whose mission is to determine whether gaps in or inconsistencies between best practices for acute and chronic pain management exist and to propose updates and recommendations to those best practices. The task force consists of experts who have significant experience across the disciplines of pain management, patient advocacy, substance use disorders, mental health, and minority health. A draft report describes preliminary recommendations of the task force that will be finalized and submitted to Congress in 2019, following a 90-day public comment period.[732]

(b) Medication Assisted Treatment

369. In addition to treatment covered by Medicaid and Medicare, SAMHSA's MAT program expanded access by providing grants to states with the highest rates of treatment admissions for opioid addiction.[733] In September 2017, SAMHSA awarded $35 million over three years in additional Medication Assisted Treatment for Prescription Drug and Opioid Addiction ("MAT-PDOA") grants to six states.[734] The fiscal year 2018 budget for the program was $95.2 million; the fiscal year 2019 budget is $100.2 million.[735] As of 2015, relevant stakeholders no longer felt cost to be the largest barrier to expansion of MAT in Ohio; rather, anti-pharmacotherapy attitudes, community opposition, physician capacity, and concerns about diversion dominated discussion on barriers to MAT expansion.[736]

---

731 "Comprehensive Opioid Abuse Program (COAP)," Bureau of Justice Assistance, https://www.bja.gov/ProgramDetails.aspx?Program_ID=72.

732 "Draft Report on Pain Management Best Practices: Updates, Gaps, Inconsistencies, and Recommendations," HHS, https://www.hhs.gov/ash/advisory-committees/pain/reports/2018-12-draft-report-on-updates-gaps-inconsistencies-recommendations/index.html.

733 "State Grant Programs," SAMHSA, https://www.samhsa.gov/medication-assisted-treatment/training-materials-resources/state-grant-programs#mat-pdoa.

734 "Addressing the Opioid Crisis in America: Prevention, Treatment, and Recovery," Senate Committee on Appropriations, https://www.appropriations.senate.gov/imo/media/doc/120517-Joint-HHS-Witnesses-Statement.pdf, p. 4.

735 "The Substance Abuse and Mental Health Services Administration Operating plan for FY 2019," SAMHSA, https://www.samhsa.gov/sites/default/files/samhsa_fy2019_operating_plan_508.pdf.

736 Molfenter, Todd et al., "Barriers to Buprenorphine Expansion in Ohio: A Time-Elapsed Qualitative Study," *Journal of Psychoactive Drugs*, 31:1, 2019, pp. 1-7.

(c) Naloxone Administration and Distribution

370. SAMHSA's Opioid Overdose Prevention Toolkits equip communities and local governments with material to develop policies and practices to help prevent opioid-related overdoses and deaths. They also serve as a foundation for educating and training.[737]

371. SAMHSA's First Responders Grant Program aims to reduce the number of deaths and adverse events related to opioids and other prescription drugs. In fiscal year 2017 (the first year of this program), SAMHSA awarded 21 grants to states or other entities, including three grants to Ohio organizations, to train first responders (and others) on implementing secondary prevention strategies, such as the administration of naloxone through FDA-approved delivery devices to reverse the effects of opioid overdose.[738] Anticipated total funding for the program in fiscal year 2019 is $16.5 million, of which approximately $9 million will be for recipients serving rural communities with high rates of opioid abuse. Applications are due May 6, 2019.[739]

372. COAP grants provide services relating to training and resources for first responders to administer opioid overdose reversal drugs like naloxone. COAP grants also are provided to support overdose outreach projects, which can connect overdose survivors with treatment and recovery services, and educate communities on overdose prevention.[740] The DOJ Bureau of Justice Assistance

---

737 "Opioid Overdose Prevention Toolkit," SAMHSA, https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA18-4742.

738 "Targeted Capacity Expansion: Medication Assisted Treatment – Prescription Drug and Opioid Addiction," https://www.samhsa.gov/grants/grant-announcements/ti-18-009; "Initiating Medication Assisted Treatment of Opioid Addiction in the Emergency Department: The ED MAT Protocol," https://www.samhsa.gov/grants/awards/2019/TI-18-009.

739 "First Responders-Comprehensive Addiction and Recovery Act," SAMHSA Announcement, March 6, 2019, https://www.samhsa.gov/grants/grant-announcements/ti-19-004.

740 "Who covers law enforcement overdose response costs?," National Training and Technical Assistance Center, https://bjatta.bja.ojp.gov/naloxone/who-covers-law-enforcement-overdose-response-costs.

("BJA") is expected to administer $145 million in fiscal year 2019 funding for COAP.[741]

373. BJA's Byrne Justice Assistance Grants ("JAG") and ONCDP's High Intensity Drug Trafficking Area ("HIDTA") Grants also may be used to equip officers with naloxone and train them in overdose reversal and prevention. Personnel training costs are typically covered from departments' operational budgets, but limited funding for overtime expenditures may be available through state and federal grants.[742] Fiscal year 2017 funding for JAG was $403 million. In fiscal year 2019, the BJA has $415.5 million in available funding for JAG, which is $159.5 million above the total funding awarded in fiscal year 2018.[743] Of the total funding available for formula grant awards under the Byrne JAG program, 60 percent is allocated for awards to states, and the remaining 40 percent supports awards to local and tribal governments.[744] ONDCP's funding for HIDTA for fiscal year 2017 was $254 million; funding for fiscal year 2018 and fiscal year 2019 was $280 million in each year.[745]

(d) Detoxification Programs

374. SAMHSA's Substance Abuse Prevention and Treatment Block Grant ("SAPT Block Grant") provides federal funding to states to prevent and treat substance abuse disorders according to a formula. Each state may distribute funds to local government entities in accordance with a required state plan for providing substance use disorder prevention and treatment services. States are given

741 "Comprehensive Opioid Abuse Program (COAP)," BJA, https://www.bja.gov/ProgramDetails.aspx?Program_ID=72; "FY 2020 Program Summaries," DOJ, Office of Justice Programs, March 2019, https://www.justice.gov/jmd/page/file/1150341/download, pp. 43-45.

742 "Who covers law enforcement overdose response costs?," National Training and Technical Assistance Center, https://bjatta.bja.ojp.gov/naloxone/who-covers-law-enforcement-overdose-response-costs.

743 "FY 2020 Program Summaries," DOJ, Office of Justice Programs, March 2019, https://www.justice.gov/jmd/page/file/1150341/download, pp. 27-28.

744 "FY 2019 Performance Budget," DOJ, https://www.justice.gov/jmd/page/file/1034426/download, p. 52.

745 "FY 2019 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2019/02/FY-2019-L-HHS-DOJ-ONDCP-Final-Appropriations-.pdf, p. 17.

flexibility in the use of SAPT funds within the framework of the state plan and federal requirements.[746] Federal funding for the SAPT Block Grant has remained level for fiscal year 2019 at $1,858 million.[747] In fiscal year 2018, Ohio was awarded $64.8 million in SAPT Block Grant formula funding.[748]

(e) Inpatient and Outpatient Therapy

375. With respect to inpatient and outpatient therapy, SAMHSA administers the two main opioid grant programs: the State Targeted Response and the State Opioid Response grants. The State Targeted Response program was authorized in the 21st Century Cures Act and is intended to close the treatment gap between those who seek treatment and those who receive it. The State Opioid Response program is intended to build on the State Targeted Response program by increasing access to MAT, reducing unmet treatment need, and reducing opioid related deaths through prevention, treatment, and recovery activities for those with opioid use disorder. The funding opportunity announcement for these programs requires that applications for funding include the entire continuum of care, prevention, treatment, and recovery. In addition, programs receiving funds under the State Opioid Response program are required to make MAT available.

376. State Targeted Response funds were awarded to states based on a formula; $500 million was awarded to states in each of fiscal year 2017 and fiscal year 2018. In 2018, Ohio received approximately $26 million in State Targeted Response funding.[749] The grant application specifies that no less than 80 percent of the award must fund treatment services. The State Opioid Response program was

---

746 "Substance Abuse Prevention and Treatment Block Grant," SAMHSA, https://www.samhsa.gov/grants/block-grants/sabg; "The Opioid Epidemic and Federal Efforts to Address It: Frequently Asked Questions," Congressional Research Service, October 18, 2017, https://www.hsdl.org/?view&did=805271, p. 10.

747 "The Substance Abuse and Mental Health Services Administration Operating plan for FY 2019," SAMHSA, https://www.samhsa.gov/sites/default/files/samhsa_fy2019_operating_plan_508.pdf.

748 "Ohio Summaries FY 2018," SAMHSA, https://www.samhsa.gov/grants-awards-by-state/OH/2018."

749 "HHS provides states second installment of grant awards to combat opioid crisis," HHS, April 18, 2018, https://www.hhs.gov/about/news/2018/04/18/hhs-provides-states-second-installment-grant-awards-combat-opioid-crisis html.

awarded to states in fiscal year 2018 and fiscal year 2019. The State Opioid Response program offers $1.4 billion in funding with 15 percent set aside for states with the highest rate of drug overdose deaths. Ohio received $56 million in funding under the State Opioid Response program in 2018,[750] and is expected to receive more than $29 million in 2019.[751] The State Targeted Response and State Opioid Response programs combined made up 21 percent of total opioid-related appropriations in fiscal year 2018.[752]

377. SAMHSA's Center for Substance Abuse Prevention Improving Access to Overdose Treatment program awards funds to Federally Qualified Health Centers, opioid treatment programs, or practitioners who have a waiver to prescribe buprenorphine. The program aims to expand access to FDA-approved drugs or devices for emergency treatment of opioid overdoses. Recipients will partner with other prescribers at the community level to develop best practices for prescribing FDA-approved overdose reversal drugs. After developing best practices, the recipients will train other prescribers in key community sectors as well as individuals who support persons at high risk for overdose.[753] This program was funded at $1 million in each of fiscal year 2018 and fiscal year 2019.[754]

---

750 "Tracking Federal Funding to Combat the Opioid Crisis," Bipartisan Policy Center, https://bipartisanpolicy.org/wp-content/uploads/2019/03/Tracking-Federal-Funding-to-Combat-the-Opioid-Crisis.pdf, p. 47.

751 "HHS releases additional $487 million to states, territories to expand access to effective opioid treatment; 2019 SOR grants will total $1.4 billion," HHS, March 20, 2019, https://www.hhs.gov/about/news/2019/03/20/hhs-releases-additional-487-million-to-states-territories-to-expand-access-to-effective-opioid-treatment.html.

752 "Tracking Federal Funding to Combat the Opioid Crisis," Bipartisan Policy Center, https://bipartisanpolicy.org/wp-content/uploads/2019/03/Tracking-Federal-Funding-to-Combat-the-Opioid-Crisis.pdf, p. 13.

753 "Apply Now: Improving Access to Overdose Treatment Program," Community Success, https://www.communitysuccess.org/apply-now-improving-access-to-overdose-treatment-program/.

754 "The Substance Abuse and Mental Health Services Administration Operating plan for FY 2019," SAMHSA, https://www.samhsa.gov/sites/default/files/samhsa_fy2019_operating_plan_508.pdf; "FY 2019 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2019/02/FY-2019-L-HHS-DOJ-ONDCP-Final-Appropriations-.pdf, p.4.

378. Medicare Part A (hospital), Part B (medical) insurance programs, and Part D prescription plans, provide coverage for drug rehab treatment. These programs cover inpatient and outpatient programs and medications used in the treatment of substance use disorders (with the exception of methadone). They also cover partial hospitalization treatment, which provides some of the services of inpatient treatment, such as individual and group therapy, family therapy, and medications. If an individual is covered by Medicare, either by age or because of disability status, these options are available. Medicaid coverage for substance use disorders, on the other hand, depends on the state, though as noted above many states have expanded Medicaid through the ACA.[755] I understand that the Bialecki Report states that treatment for opioid use disorders in the Counties is funded by Medicaid, with a certain percentage funded by the Counties' Alcohol, Drug Addiction & Mental Health Services Boards ("ADM Boards").

(f) Recovery Housing

379. The U.S. Department of Agriculture ("USDA") and HHS announced on February 15, 2019, that they will partner to create addiction recovery housing in rural communities. Nonprofit organizations will be able to purchase homes from USDA and convert them into transitional housing for people recovering from opioid misuse.[756]

380. For fiscal year 2017 (the first year of the program), SAMHSA awarded eight grants under its Building Communities of Recovery grant program to recovery-focused community organizations. Grantees are to use the funds to develop, expand, and enhance recovery support services such as peer support services and

[755] "Public Assistance Options for Drug and Alcohol Treatment Centers," American Addiction Centers, https://americanaddictioncenters.org/rehab-guide/public-assistance.

[756] "USDA and HHS Partner to Create Recovery Housing in Rural Communities," SAMHSA Press Announcement, February 15, 2019, https://www.samhsa.gov/newsroom/press-announcements/201902151000.

linkages to other services. For fiscal year 2019, SAMHSA announced funding to be $521,000.[757]

(g) SBIRT and STIR Programs for Adolescents

381. Screening, Brief Intervention, And Referral To Treatment ("SBIRT") is a comprehensive, integrated, public health approach to the delivery of early intervention and treatment services for persons with substance use disorders, as well as those, such as adolescents, who are at risk of developing these disorders. Primary care centers, hospital emergency rooms, trauma centers, and other community settings provide opportunities for early intervention with at-risk substance users before more severe consequences occur. Screening quickly assesses the severity of substance use and identifies the appropriate level of treatment. Brief intervention focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change. Referral to treatment provides those identified as needing more extensive treatment with access to specialty care.[758] Fiscal year 2018 funding was $24.7 million and fiscal year 2019 funding is $30 million.[759] From 2013-2018, SAMHSA's Center for Substance Abuse Treatment ("CSAT") funded a state cooperative agreement with Ohio in addition to funding SBIRT Medical Professional Training grants with Ohio universities from 2013-2016.[760]

382. Screening, Treatment Initiation and Referral ("STIR") is a recent modification of SBIRT that includes MAT for opioid dependent patients, including adolescents. It involves establishing a clear method of follow-up with patients that have been

---

757 "Building Communities of Recovery," SAMHSA Announcement, February 1, 2019, https://www.samhsa.gov/grants/grant-announcements/ti-19-003.

758 "About Screening, Brief Intervention, and Referral to Treatment (SBIRT)," SAMHSA, https://www.samhsa.gov/sbirt/about.

759 "The Substance Abuse and Mental Health Services Administration Operating plan for FY 2019," SAMHSA, https://www.samhsa.gov/sites/default/files/samhsa_fy2019_operating_plan_508.pdf.

760 "Screening, Brief Intervention, and Referral to Treatment (SBIRT) Grantees," SAMHSA, https://www.samhsa.gov/sbirt/grantees#Grantee Websites.

identified as having a possible dependency on a substance or in need of specialized treatment.[761]

383. In its annual funding considerations for fiscal year 2018, the House Committee on Appropriations report stated:

> The Committee provides $30,000,000 for Screening, Brief Intervention and Referral to Treatment, which is the same as the fiscal year 2017 enacted program level, and $16,804,000 below the fiscal year 2018 budget request program level. Within this amount, the Committee provides $1,000,000 for grants to pediatric health care providers in accordance with section 9016 of the 21st Century Cures Act (P.L. 114–255). Grants should focus on screening for underage drinking, opioid use, and other drug use. The Committee understands that substance use disorders, including opioid use, typically begin in adolescence, and that preventing underage drinking and other early substance use is a cost-effective strategy in preventing costly problems later in life.[762]

384. For the fiscal year 2019 funding considerations, the Senate Committee on Appropriations report also stated:

> The Committee recognizes that SBIRT is still not widely adopted and has not yet permeated broader healthcare or social service networks, particularly in underserved communities most affected by the opioid epidemic. The Committee encourages SAMHSA to use funds for the adoption of SBIRT protocols in primary care and other appropriate settings that serve youth 12 to 21 years of age as well as on the adoption of system-level approaches to facilitate the uptake of SBIRT into routine health care visits for adults.[763]

E. Overview of Additional Harm Reduction Programs Offered by the Federal Government

385. Additional harm reduction programs provided and/or funded by the U.S. Government include HIV and Hepatitis C interventions for intravenous drug

---

761 "Referral to Treatment," SAMHSA-HRSA Center for Integrated Health Solutions, https://www.integration.samhsa.gov/clinical-practice/sbirt/referral-to-treatment.

762 "FY 2018 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2017/08/FY-2018-House-Approps-August-2017.pdf.

763 "FY 2019 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2019/02/FY-2019-L-HHS-DOJ-ONDCP-Final-Appropriations-.pdf.

users, syringe exchange services, routine clinical fentanyl toxicology testing, and housing support. Each of these programs is briefly addressed in turn.

(a) Interventions to Treat and Reduce Spread of HIV and Hepatitis C among Intravenous Drug Users

386. The CDC funds various programs to reduce the spread of hepatitis throughout the nation.[764] CDC programs work to implement evidence-based drug prevention in school and community settings, and to stop the spread of infectious diseases like HIV and hepatitis C among people who inject drugs.[765]

387. For fiscal year 2019 funding, the House and Senate Appropriations Conference Report stated: "The conferees direct CDC to focus efforts on improving surveillance, treatment, and education efforts around hepatitis B, hepatitis C, and HIV infections as it relates to the opioid epidemic. The CDC is directed to prioritize funding for those areas most at risk for outbreaks of HIV and hepatitis due to injection drug use."[766] This is a new program with fiscal year 2019 funding at $5 million.[767]

388. CSAT's fiscal year 2019 Minority AIDS Initiative provides substance use disorder treatment for racial/ethnic minority populations at high risk for HIV/AIDS. The purpose of this program is to increase engagement in care for racial and ethnic minority individuals with substance abuse disorder and/or co-occurring substance use and mental disorders who are at risk for HIV or are HIV

764 "Funded Partners/Programs and Budgets," CDC, https://www.cdc.gov/hepatitis/policy/fundedpartners.htm.

765 "Infectious Diseases, Opioids and Injection Drug Use," CDC, https://www.cdc.gov/pwid/opioid-use.html.

766 "FY 2019 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2019/02/FY-2019-L-HHS-DOJ-ONDCP-Final-Appropriations-.pdf.

767 "FY 2019 Appropriations," The National Association of State Alcohol and Drug Abuse Directors, http://nasadad.org/wp-content/uploads/2019/02/FY-2019-L-HHS-DOJ-ONDCP-Final-Appropriations-.pdf.

positive and receive HIV services/treatment. Total available funding is $12 million and the anticipated award amount is $500,000 for up to five years.[768]

(b) Syringe Exchange Services

389. Under the CDC HIV program, CDC partners with HHS to fund and guide syringe exchange programs at the state level.[769] The CDC Program Guidance for Implementing Certain Components of Syringe Services Programs, 2016, provides a roadmap for state syringe exchange programs.[770]

(c) Routine Clinical Toxicology Testing for Fentanyl

390. The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act became law in October 2018. This effort to combat the opioid crisis follows the passage of CARA and the 21st Century Cures Act. The bill establishes and expands programs to support increased detection and monitoring of fentanyl and other synthetic opioids, including a new grant program for public health laboratories and a pilot program for point-of-use drug testing. The legislative package directs funding to federal agencies and states so they can make increasing access to addiction treatment a priority and sets in place interventions to help mitigate the crisis, such as preventing over-prescription.[771]

(d) Housing Support

391. SAMHSA's Services in Supportive Housing ("SSH") program helps prevent and reduce chronic homelessness by funding services, in conjunction with permanent housing, for individuals and families experiencing homelessness and living with a severe mental and/or substance use disorder. Grants are awarded competitively

768 "Minority Aids Initiative: Substance Use Disorder Treatment for Racial/Ethnic Minority Populations at High Risk for HIV/AIDS," SAMHSA Announcement, February 21, 2019, https://www.samhsa.gov/grants/grant-announcements/ti-19-008.

769 "Syringe Services Programs," CDC, https://www.cdc.gov/hiv/risk/ssps html.

770 "Centers for Disease Control and Prevention (CDC) Program Guidance for Implementing Certain Components of Syringe Services Programs, 2016," CDC, https://www.cdc.gov/hiv/pdf/risk/cdc-hiv-syringe-exchange-services.pdf.

771 H.R.6 - SUPPORT for Patients and Communities Act (Public Law No: 115-271), § 7011.

for up to five years to community-based public or nonprofit entities. Services supported under SSH funding include, but are not limited to, outreach and engagement, intensive case management, and mental health and substance abuse treatment.[772]

392. SAMHSA's Grants for the Benefit of Homeless Individuals ("GBHI") is a competitively awarded grant program that enables communities to expand and strengthen their treatment services for people experiencing homelessness. Grants are awarded for up to five years to community-based public or nonprofit entities and fund programs and services including substance abuse treatment, mental health services, immediate entry into treatment, outreach services, screening and diagnostic services, staff training, case management, primary health services, job training, educational services, and relevant housing services.[773] The GBHI program is a competitive grant program administered by CSAT. GBHI grants are awarded in two categories, GBHI and GBHI-SSH.[774] The SAMHSA GBHI fiscal year 2017 grant announcement anticipated $9.5 million for up to 24 awards up to five years.[775]

F. Costs Associated with Certain Diagnoses

393. Plaintiffs have submitted expert reports setting out estimated abatement costs that may be incurred by the Counties in future years. For example, the Liebman Report provides estimates of costs in the categories of treatment, harm reduction, and prevention, for both of the Counties.[776] The treatment cost appears to be based on an estimated cost of approximately $24,000 per person (not including

772 "Grants," HHS, https://www.hhs.gov/programs/social-services/homelessness/grants/index html; "Behavioral Health," Youth.gov, https://youth.gov/youth-topics/runaway-and-homeless-youth/behavioral-health.

773 "Grants," HHS, https://www.hhs.gov/programs/social-services/homelessness/grants/index html.

774 "Grants for the Benefit of Homeless Individuals (GBHI)," SAMHSA, https://www.samhsa.gov/homelessness-programs-resources/grant-programs-services/gbhi-program.

775 "Grants for the Benefit of Homeless Individuals," SAMHSA Announcement, February 23, 2017, https://www.samhsa.gov/grants/grant-announcements/ti-17-009.

776 Liebman Report, Tables 1 and 2.

MAT services).[777] Plaintiffs also have submitted expert reports setting out estimated NAS treatments in the Counties at estimated costs of $9.4 million in Cuyahoga County and $6.7 million in Summit County.[778]

394. I note that treatment for opioid use disorders is covered by Medicaid, wherein a percentage is covered by the Counties' ADM Boards, as I understand is described in the Bialecki Report. As such, it is not apparent that there are any such additional treatment costs to be borne by the Counties. Nonetheless, I have been asked to consider how cost estimates derived from the Ohio Medicaid Data compare with the estimates noted above.[779]

395. I consider costs attributable to a diagnosis of opioid abuse, dependence, or overdose. I select Medicaid beneficiaries for whom the first opioid abuse, dependence, or overdose diagnosis appears in the data and who were continuously eligible for Ohio Medicaid benefits for one year before and one year after the diagnosis. Over the period 2011 to 2017, 23,382 Ohio Medicaid recipients received an opioid abuse, dependence, or overdose diagnosis. The median cost incurred by Ohio Medicaid in the 12 months following the first such event was $11,075; the distribution of these costs is shown in Exhibit X-2. As these costs include some costs that would have been incurred even in the absence of the triggering event, I also compute for these same individuals the cost incurred by Ohio Medicaid in the 12 months preceding the opioid abuse, dependence, or overdose diagnosis. I define the incremental cost as the cost in the 12-month period after the opioid abuse, dependence, or overdose diagnosis (including the cost on the date itself) less the cost incurred on behalf of the individual in the 12 months before the diagnosis.

---

777 Liebman Report, Table C.1.

778 Report of Professor Thomas McGuire Regarding Public Nuisance, March 25, 2019 ("McGuire Report"), ¶ 122. See also Wexelblatt Report, Section III.D.

779 For the purposes of this discussion, I use costs associated with payment of Ohio Medicaid claims to be a proxy for any costs directly associated with the conditions at issue that may be paid by the Counties.

396. Summary statistics based on this incremental cost are shown in Exhibit X-2. The median incremental cost is $2,663; as can be seen from the distribution of costs, a significant fraction of patients (more than 25 percent) are associated with a negative incremental cost.

397. While Plaintiffs have provided information on infants born with NAS in the Counties, it should be noted that most infants with NAS are Medicaid beneficiaries and, accordingly, would not impose medical costs on the Counties.[780] I am also aware that NAS may arise due to drugs other than opioids.[781]

398. Plaintiffs have also submitted expert reports suggesting that as they develop, children with NAS may need special services.[782] Plaintiffs' experts do not, however, purport to identify costs for such services for the Counties.[783] Further, certain federal programs exist for infants and children with NAS.[784] In addition, I understand that state and/or local programs relating to NAS are addressed in the Bialecki Report.

---

780 See Wexelblatt Report, Table 1, Medicaid Discharge versus Non-Medicaid Discharge. According to Dr. Wexelblatt, seven of eight NAS infants diagnosed in Ohio since 2011 are covered by Medicaid (Deposition of Scott Wexelblatt, M.D., April 24, 2019, p. 49).

781 See e.g., "Neonatal Abstinence Syndrome," Semel Institute for Neuroscience and Human Behavior, UCLA, https://www.semel.ucla.edu/dual-diagnosis-program/News_and_Resources/Neonatal_Abstinence_Syndrome.

782 See Keyes Report, p. 25; McGuire Report, ¶ 120; Wexelblatt Report, ¶¶ 49-51.

783 See McGuire Report, ¶ 120.

784 In February 2018, HRSA was allocated $400 million through fiscal year 2022 to award grants to states, territories, and tribal communities to promote, among other things, child development and school readiness among children with NAS ("The Maternal, Infant, and Early Childhood Home Visiting Program," https://mchb hrsa.gov/sites/default/files/mchb/MaternalChildHealthInitiatives/HomeVisiting/pdf/programbrief.pdf; "HRSA's Home Visiting Program: Supporting Families Impacted by Opioid Use and Neonatal Abstinence Syndrome," https://mchb.hrsa.gov/sites/default/files/mchb/MaternalChildHealthInitiatives/HomeVisiting/MIECHV-Opioid-NAS-Resource.pdf.

Gregory K. Bell

May 10, 2019

APPENDIX A:
Data Appendix

I. ARCOS DATA

A. Data Import and Cleaning

1. For the purpose of these proceedings, I understand that the DEA produced raw data from ARCOS (the "ARCOS Data") which "monitors the flow of DEA controlled substances from their point of manufacture through commercial distribution channels."[1] The ARCOS Data covers the period 2006-2014, for all 50 states plus the armed services and US territories and includes all products related to one of the following underlying ingredients: buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, powdered opium, oxycodone, oxymorphone, and tapentadol.

2. Each observation in the ARCOS Data contains information on the "reporter" – the entity from which the controlled substance is being purchased (and correspondingly, the entity required to report the transaction to the DEA) – and the "buyer" – the entity purchasing the controlled substance. For the purposes of my analyses, I limit the ARCOS Data to shipments made to what I classify as "patient-facing" users; that is, entities whose purpose is to distribute these products to patients. Accordingly, I exclude from my analyses buyers that are classified as one of the following types: analytical lab, distributor, exporter, importer, manufacturer, researcher, and reverse distributor.[2]

3. The ARCOS Data contain several variables describing the relevant transaction. These variables include the "transaction code", which described the type of the transaction, as the well as the number of units ("units"), dosage units ("dosage units"), and anhydrous weight ("grams") associated with each order. When the

[1] "Background: What is ARCOS and What Does it Do?" DEA, https://www.deadiversion.usdoj.gov/arcos/index.html.

[2] These transactions represent 5.6 percent of the sample.

sample is limited as described in the paragraph above, there are only 5 possible transaction codes: "S" (sale), "P" (purchase), "R" (return), "V" (unsolicited return), and "X" (lost in transit). For the purpose of my analyses I drop all observations with the transaction code "X" or lost in transit.[3] Also for the purpose of my analyses, I multiply each of the three quantity variables by (-1) if the transaction represents a shipment from the buyer to the reporter; thus, all transactions with transaction codes of "P", "V", or "R" are multiplied by (-1).[4]

4. Upon review of the ARCOS data, several data-entry errors were discovered. These entries often had values for a quantity-related variable (total weight, total quantity in units, and dosage units) that was inconsistent with the other two variables. In these instances, I adjusted to figures consistent with the observed ratios from other observations with the same NDC codes. A full list of adjustments can be found in my backup materials.

5. Further, it is apparent that certain observations associated with different DEA numbers correspond to the same buyer or buyer location in Cuyahoga and Summit Counties. For physicians, I consolidate different buyer DEA numbers for the same physician in the same county. For pharmacies, I consolidate different buyer DEA numbers for the same pharmacy location. For hospitals and clinics, I also consolidate different buyer DEA numbers for the same location. A full list of adjustments can be found in my backup materials.

B. MME

6. To convert an order to its Morphine Milligram Equivalent (MME), I multiply the weight of the order (converted to milligrams) by the molecules MME conversion factor. All MME conversion factors are listed in III-1. A similar methodology was also used by the Plaintiffs' experts.

---

[3] These transactions represent less than 0.001 percent of the sample

[4] "Purchases" in ARCOS represent a decrease in inventory on the part of the buyer (See "ARCOS Registrant Handbook," Office of Diversion Control, 1997, https://www.deadiversion.usdoj.gov/arcos/handbook/full.pdf#search=registrant%20handbook, pp 86-87).

7. No MME value was calculated for any product whose main ingredient is buprenorphine.

II. IQVIA XPONENT DATA

A. Data Import and Cleaning

8. Prescribing data from IQVIA ("IQVIA Xponent Data") was produced by Allergan in conjunction with these proceedings (ALLERGAN_MDL_02485011; ALLERGAN_MDL_03281086; GPS_084_73_non-USC022_mkt_def_JUL2018; GPS_084_71_USC022_mkt_def_APR2018). ALLERGAN_MDL_02485011 and ALLERGAN_MDL_03281086 contain prescribing information between 1997 and 2018 at the level of the prescriber – "product group" – payor (post 2007 only) – zip code – channel – month – year level.[5] Product groups are classes of products; a description of the products in each product group can be found in GPS_084_73_non-USC022_mkt_def_JUL2018 and GPS_084_71_USC022_mkt_def_APR2018. For each relevant observation, IQVIA provides four quantity variables: total and new prescriptions, and total and new quantity. The former refers to the number of prescriptions while the latter refers to the number of dosage units ("total" figures include amounts associated with refill prescriptions). I understand that quantities are projected estimates based on the data collected by IQVIA.

9. The IQVIA data contained two zip code variables: "prescriber zc" and "prescriber zip". The former appeared to relate to the actual address of the prescriber; the latter relates to the overall prescriber identifier. I use "prescriber zc" to represent the location of a prescriber; however, in the few instances in which this variable missing, I use "prescriber zip" instead. These two variables, "prescriber zip" and "prescriber zc", were identical in 98.6 percent of instances.

[5] ALLERGAN_MDL_02949563-64 at 64.

B. MME

10. In order to convert the quantity data from IQVIA to MME, I extract the strength for each product group from the corresponding product group files, [GPS_084_73_non-USC022_mkt_def_JUL2018.xlsx and GPS_084_71_USC022_mkt_def_APR2018.xlsx]. These files contain 2 columns, "product name" and "product description," that contain information related to the molecule, strength, form, and package size associated with each product. In cases of combination products, often multiple strengths were provided without identifying which strength specifically corresponded to the opioid. In these instances, manual adjustments were made based on consultation with other databases, such as the FDA and CDC.

11. Once the strength for each product is known, I calculate MME using formula of strength × dosage units × MME conversion factor. MME conversion factors are the same as those discussed above. All product groups whose base molecule was buprenorphine was excluded from the analyses.

III. OARRS DATA

A. Data Import and Cleaning

12. For the purpose of these proceedings, I understand that the Ohio BOP produced a data extract from OARRS covering the period from 2008 through 2018 ("OARRS Data"). The OARRS Data contain prescription-level information on prescriptions such that: (i) the prescriber is located in the Counties; (ii) the pharmacy is located in the Counties; or (iii) the patient resides in the Counties. Information contained in the OARRS Data include patient, prescriber, and pharmacy identifiers (anonymized); the NDC number associated with each prescription; the name and description of the drug; the days' supply; the total dosage units; the age of the patient; and the number of authorized refills. Furthermore, for each of the

prescriber, pharmacy, and patient, the OARRS Data provide the first three digits of the entity's zip code.[6]

13. I impose several restrictions on the OARRS Data before conducting my analyses. First, I drop all non-opioids from the OARRS Data. Second, I drop all prescriptions for individuals under the age of 15. Third, I drop all observations with a negative quantity of dosage units or a negative number of authorized refills. Fourth, I drop all NDC codes whose base molecule is naloxone, naltrexone, or buprenorphine. The end result is a dataset with information on over 24 million prescriptions.

B. MME

14. In order to convert a prescription quantity to MME, I use strength information at the NDC code level from the CDC. I calculate MME as strength × dosage units × MME conversion factor. The MME conversion factors are the same as those discussed above. In order to assign the correct MME conversion factor, I require information on the underlying molecule as well as the formulation of the drug. The former was extracted from the "Therapeutic Class Code" variable and latter from the "Drug" variable, both in the OARRS Data.

IV. OHIO MEDICAID DATA

A. Data Import and Cleaning

15. For the purpose of these proceedings, I understand that the Ohio Department of Medicaid produced an extract of Ohio Medicaid claims data for the years 2010 through 2018 ("Ohio Medicaid Data"). The Ohio Medicaid Data include all claims involving: (i) a resident of the Counties; or (ii) a prescriber located in the Counties; or (iii) a pharmacy located in the Counties. The data are restricted to all Ohio Medicaid claims associated with Ohio Medicaid beneficiaries who had been

[6] I understand that all observations in 3-digit zip codes where there were 10 or fewer pharmacies or prescribers are excluded from the OARRS Data.

prescribed an opioid during the 2010-2018 period or had been diagnosed with an opioid-related ICD-9 or ICD-10 code during the 2010-Oct/2018 period.[7] A list of the NDC codes used to flag opioid prescriptions is Attachment 1 – NDC Codes.xlsx; a list of the ICD-9 and ICD-10 codes used to flag opioid-related diagnoses is Attachment 2 – ICD-9 and ICD-10 Codes.

16. The Ohio Medicare Data contains claims submitted to Ohio Medicaid, some of which are denied. For my analyses, I consider only claims accepted by Ohio Medicaid. In addition, I understand that a claim may be erroneously processed by Ohio Medicaid multiple times and hence assigned different ICNs (internal control number assigned to a claim when processed in the MITS interChange system) and paid dates. Claims that have the same information except for ICN and paid date are de-duplicated by only keeping the earliest claim. Additionally, in pharmacy claims where dispensed quantity is present, a few claims in 2012 have dispensed quantity exceeding 1,000, inconsistent with the cost and unit price, or the strength, days of supply, and clinically recommended daily dosage of the same claim. By dividing these dispensed quantities by 1,000, I restore consistency with other observations.

B. MME

17. I do not have MME conversion factors for diphenoxylate, difenoxin, paregoric, sufentanil citrate, or remifentanil, hence these opioids are not included when I sum each beneficiary's total MME. Few beneficiaries ever used these opioids; for example, only 8,482 beneficiaries ever used diphenoxylate, the most frequently used opioid of this list, accounting for less than 2 percent of all opioid-using beneficiaries in the Ohio Medicaid Data. Additionally, for fentanyl, not all formulations have an available MME conversion factor. In these instances, I use the median MME conversion factor of all fentanyl claims with known MME

[7] The Ohio Medicaid Data includes an eligibility table that flags if a beneficiary is eligible for Ohio Medicaid benefits for each month of the 2010–October 2018 time period.

conversion factors in the Ohio Medicaid data as the imputed MME conversion factor.

C. Definitions of Abuse, Dependence, and Overdose

18. Of the ICD-9 and ICD-10 diagnosis codes related to opioid abuse/dependence/overdose, I separate overdose from abuse/dependence by identifying codes for opioid-related poisoning as overdose. The heroin overdose codes identify a sub-category of interest; ICD-9 code 965.01, E850.0 and ICD-10 code T40.1 are classified as heroin overdose. These heroin overdose codes are combined with ICD-9 code 965.0, 965.00, 965.02, 965.09, 970.1, E850.1, E850.2, E950.0, E980.0 and ICD-10 code T40.0, T40.2, T40.3, T40.4, T40.6, T50.7 to represent opioid overdose. The remaining codes in the list of those related to opioid abuse/dependence/overdose are classified as opioid abuse/dependence.

D. Other Diagnosis Groupings

19. To identify beneficiary-specific drivers of opioid abuse/dependence/overdose diagnoses such as other substance abuse behaviors and psychiatric disorders, I use ICD-9/10 codes and beneficiary medical claims. For substance abuse behaviors, I use ICD-9/10 codes for Alcohol Abuse. For psychiatric disorders, I use ICD-9/10 codes for Anxiety, Depression, Bipolar Disorder, Schizophrenia, and PTSD.

V. MCKESSON SHIPMENT DATA

20. I am provided data from McKesson regarding its shipments of controlled substances (MCKMDL00711905; MCKMDL00711907; MCKMDL00478913; MCKMDL00579972; MCKMDL00606062) and non-controlled substances (MCKMDL00711904; MCKMDL00711906) to Cuyahoga and Summit Counties from October 2004 to June 2018 ("McKesson Data").[8] Each observation in the McKesson Data corresponds to a shipment from McKesson to a customer of a drug and contains customer, transaction, and product details. Customer

[8] For non-controlled products, the data include shipments from June 2004 to November 2017; for controlled products, the data include shipments from September 2004 to June 2018.

information includes the customer's DEA number, account number, name, and address. Transaction information includes the bill date and sales order date. The transaction's product information includes the product's NDC number, material number, material description, base code (for controlled substances), billed quantity, and the number of doses of the product in the shipment. The McKesson Data also includes returns as indicated by negative quantities.

21. As I discussed with the ARCOS Data, different DEA numbers may correspond to the same pharmacy location or hospital / clinic location. I consolidate different buyer DEA numbers for the same location. A full list of adjustments is in my backup materials. In considering shipments to pharmacies, I only consider those pharmacies with net positive shipments of opioids and non-controlled substances in the calendar year.

VI. CARDINAL SHIPMENT DATA

22. I am provided data from Cardinal regarding its shipments to Cuyahoga and Summit Counties of controlled and non-opioid controlled substances (CAH_MDL2804_00617997; CAH_MDL2804_00059301) from 2006 to 2017 and of opioid substances (CAH_MDL2804_03263593) from 1996 to 2018 {"Cardinal Data"). The Cardinal Data contain several variables describing each transaction. Each observation corresponds to a shipment from Cardinal to a customer of a drug and contains customer, transaction, and product details.[9]

23. Customer information includes the customer's DEA number, name, and address. Transaction information includes invoice date and number. The transaction's product information includes the product's NDC number, description, strength, form, size, package size, base code (for controlled substances), base code description, quantity ordered, and quantity shipped. Opioid substances data include the number of doses of the product in the shipment. The number of doses

[9] The Cardinal Data also include information on the Cardinal distribution center's DEA number and location which made the shipment.

shipped was not provided for controlled and non-opioid controlled substances. I estimate doses shipped using the size and quantity shipped data provided. The Cardinal Data also include returns as indicated by negative quantities associated with those transactions.

24. As I discussed with the ARCOS Data, different DEA numbers may correspond to the same pharmacy location or hospital / clinic location. I consolidate different buyer DEA numbers for the same location. In addition, the Cardinal Data include some purchases by individual physicians. I excluded these physician purchases from the data. A full list of adjustments can be found in my backup materials.[10] In considering shipments to pharmacies, I only consider those pharmacies with net positive shipments of opioids and non-controlled substances in the calendar year.

VII. PUBLICALLY AVAILABLE DATA

A. SEER Data

25. I use publicly available data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. The SEER Program collects and publishes cancer incidence and survival data for the US population ("SEER Data"). I use SEER Data county level information on population from 1990 to 2017 to obtain estimates of the population of the U.S., Ohio, Cuyahoga County, and Summit County.[11]

B. DEA Quota Data

26. The DEA publishes annually the aggregate production quota of selected controlled substances, including oxycodone and hydrocodone, for the current year

[10] The same adjustments to buyer DEA numbers are made with respect to the ARCOS Data, McKesson Data, and Cardinal Data.

[11] "Overview of the SEER Program," NCI SEER Program, https://seer.cancer.gov/about/overview html; "Download U.S. Population Data – 1969-2017," NCI SEER Program, https://seer.cancer.gov/popdata/download html. The SEER Program's population data are based on information from the U.S. Census Bureau.

and historical information for the last ten years.[12] I use the current 2019 schedule listing information for 2009 to 2019[13] and an archived 2010 schedule listing information for 2000 to 2010.[14] Where the schedules overlap (2009 and 2010), I use the data from the 2019 schedule. The production quotas for a molecule (including oxycodone) may contain two figures. The "for conversion" quota applies in those instances where the manufacturer changes the basic drug class and the "for sale" quota applies in those instances where the manufacturer does not.[15] In calculating the annual quotas for a molecule, I combined the "for conversion" and "for sale" quotas.

C. NSDUH Data

27. The NSDUH is a survey that measures the use of illegal and prescription drugs, alcohol, and tobacco, as well as mental disorders, treatment, and co-occurring substance use. The survey has been conducted by the federal government since 1971 and collects data by surveying residents of households who are U.S. civilians, older than 12 years, and are not institutionalized. The NSDUH has been conducted every year since 1990; prior to 1990, it was only conducted every two or three years. Over time, the survey has been changed to revise questions and adjust the sampling design.[16] For the purposes of this report, I use the publicly available dataset from the NSDUH. In the exhibits to my report, I note where my analyses span years where substantive changes were made to the NSDUH.

---

12 The quota figures are reported in kilograms of anhydrous acid or base.

13 See "2019 Aggregate Production Quota History for Selected Substances," DEA Diversion Control Division, https://www.deadiversion.usdoj.gov/quotas/quota_history.pdf.

14 Internet Archive Wayback Machine, May 27, 2010, https://web.archive.org/web/20100527195030/https://www.deadiversion.usdoj.gov/quotas/quota_history.pdf.

15 "Research vs Manufacturing," Minh T. Dang, Drug Enforcement Administration UN Reporting & Quota Section, https://www.deadiversion.usdoj.gov/mtgs/man_imp_exp/conf_2013/dang_2.pdf.

16 "National Survey on Drug Use and Health," SAMHSA, HHS, https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health.

28. The NSDUH provides sample weights that I use to extrapolate the survey results to the entire population.[17] I also use, wherever possible, the imputation revised variables. The revision imputes responses to missing variables in a method consistent to other responses as well as other statistical methods in more ambiguous situations.[18]

29. I define illicit drug use as the use of heroin, hallucinogens, or cocaine,[19] or the misuse of inhalants, tranquilizers, sedatives, stimulants, or non-OTC pain relievers,[20] unless otherwise indicated.[21] By this definition, for drugs that are legal in some instances, I only consider misuse of the drug. This is relevant for inhalants, tranquilizer, sedatives, stimulants, and non-OTC pain relievers. For example, misuse of inhalants would be classified as illicit drug use. Misuse, abuse, and dependence are defined by the NSDUH.

30. In a number of instances, I restrict my analyses to 2002 to 2014 as the survey was substantively unchanged during the period. In addition from all of my analyses, I exclude ages 12-17 and consider only the "adult" population of 18 or older. When calculating the use of another drug prior to pain reliever misuse, I drop observations where the age of starting drug use is the same as the age of starting pain reliever misuse, as I cannot determine which came first.

---

17 All results are weighted using the sample weight variables ANALWT (1979-1998), ANALWC1 (2002-2014), and ANALWT_C (1999-2001, 2015, 2016, 2017).

18 For example, see "2016 National Survey on Drug Use and Health, Methodological Summary and Definitions, A.3.3 Statistical Imputation", SAMHSA,https://www.samhsa.gov/data/sites/default/files/NSDUH-MethodSummDefs-2016/NSDUH-MethodSummDefs-2016 htm#a3-3.

19 For cocaine, I include the use of crack cocaine and powder cocaine. The NSDUH sometimes refers to this just as cocaine, generally, and sometimes as "any form of cocaine". For stimulants, I include the misuse of prescription stimulants and methamphetamine.

20 For example, respondents were shown a "pill card" displaying the names and photographs of specific pain relievers and were asked to indicate which, if any, they had ever used without a doctor's prescription or simply for the feeling or experience the drug caused. The majority of the pain relievers on the pill card are opioids (see for example, the 2012 pill card used, https://www.samhsa.gov/data/sites/default/files/NSDUH2012MRB/NSDUH2012MRB/2k12PillCards.pdf).

21 I drop heroin and pain reliever from illicit drug use when use of these drug is included in the distinction between groups.

Appendix B-1

	Doctor	Address (either home address of office address)	County	Outcome	Date
[1]	Adolph Harper, Jr.	2172 Romig Road Akron, Ohio 44320	Summit	Guilty plea; license surrendered.	10/20/2014 Guilty Plea; 5/22/2012 license surrender
[2]	Brian Heim	2901 Ironwood Drive Akron, Ohio 44312	Summit	Guilty plea; license revoked.	12/12/2014 Guilty Plea; 5/8/2013 license revoked
[3]	Charles Chiedo Njoku	Akron, Ohio	Summit	Guilty plea; license suspended then revoked.	4/11/2012 license revoked; 4/13/2011 license suspended; 9/28/2010 Guilty Plea
[4]	David Carl Ernst	Metro Life Flight, Cleveland, Ohio	Cuyahoga	License suspended, reinstated, suspended, and reinstated.	8/11/2004 license suspended; 5/19/2005 license reinstated; 2/11/2009 license suspended; 5/13/2009 license reinstated
[5]	Edward N. Robertson	24755 Chagrin Blvd., Suite 145 Beachwood, Ohio 44122	Cuyahoga	Dentistry license suspended for 30 days and subsequently reinstated.	1/7/2004 license suspended
[6]	George Smirnoff	Superior Ave. Cleveland, Ohio	Cuyahoga	Guilty plea; license surrendered.	10/1/1999 Guilty Plea; 10/14/1999 license surrendered
[7]	Gregory Ingram	Akron General Medical Center, Akron, Ohio	Summit	Guilty plea; license suspended then revoked.	4/12/2017 license revoked; 8/17/2015 Guilty Plea; 7/8/2015 license suspended
[8]	Jerome Yokiel	Beachwood, Ohio	Cuyahoga	License suspended then reinstated.	11/8/2017 license suspended; 5/9/2018 probation
[9]	Joseph Francis Lydon	Cleveland, Ohio	Cuyahoga	License suspended then reinstated.	12/13/2008 license suspended; 3/14/2012 license reinstated
[10]	Juan Hernandez	5454 State Road Parma, Ohio 44134	Cuyahoga	License suspended then revoked.	9/9/2015 license suspension; 12/9/2015 Revocation of License
[11]	Keith M. Bram	25701 North Lakeland Boulevard Euclid, Ohio 44123	Cuyahoga	Dentistry license suspended and reinstated.	7/10/1997 license suspended
[12]	Lorenzo Lalli	18099 Lorain Rd., Suite #312 Cleveland, Ohio	Cuyahoga	Guilty plea; license surrendered.	2014 Guilty Plea; 11/25/2013 license surrendered
[13]	Marcellus JaJuan Gilreath	12405 Emery Ave. Cleveland, Ohio 44135	Cuyahoga	Guilty plea; license surrendered.	7/10/2013 Permanent Surrender of Certificate 7/12/2013 guilty plea
[14]	Mark S. McAllister	Cleveland Clinic Foundation, Cleveland, Ohio	Cuyahoga	License revoked, reinstated, suspended, and surrendered.	3/10/1999 licenses revoked; 6/8/2005 license reinstated; 2/13/2008 license suspension; 12/12/2012 license surrendered
[15]	Matthew D. Kellems	University Hospital, Cleveland, Ohio	Cuyahoga	License suspended then reinstated.	11/12/2009 license suspended; 10/13/2010 license reinstated
[16]	Matthew Henry Evenhouse	MetroHelath Medical Center, Cleveland, Ohio	Cuyahoga	License suspended then reinstated.	4/9/2008 license suspended; 11/12/2009 license reinstated
[17]	Michael P. Tricaso	Better Living Clinic of Akron	Summit	Court injunction on prescribing opioids or practicing medicine; license surrendered.	10/26/2018 injunction; 8/23/2018 license surrendered

Appendix B-1

[18]	Michael W. Dagostino	6681 Ridge Road, #308 Parma, Ohio 44129	Cuyahoga	Dentistry license suspended for 60 days and reinstated.	9/11/1997 license suspended
[19]	Miller, Brent L	6803 Mayfield Road, Suite 300 Cleveland, Ohio 44124	Cuyahoga	Dentistry license placed on probationary status.	12/1/2004 probation
[20]	Nancy L. Zagunis	4468 Broadview Rd. Cleveland, Ohio 44105	Cuyahoga	Dentistry license suspended for six months.	7/26/2005 license suspended
[21]	Richard Mark Weil	Akron, Ohio	Summit	License suspended then reinstated.	12/12/2008 license suspended; 11/12/2009 license reinstated
[22]	Ronald Celeste	Westlake, Ohio	Cuyahoga	Guilty plea; license permanently revoked/surrendered.	4/4/2106 Guilty Plea; 4/13/2016 license surrendered
[23]	Samuel Nigro	Cleveland, Ohio	Cuyahoga	Guilty plea; license surrendered.	4/18/2013 Guilty Plea; 6/25/2013 sentencing; 7/11/2012 license surrendered
[24]	Shane R. Hanzlik	3693 Lynnfield Rd. Shaker Hts., Ohio 44122	Cuyahoga	Training license suspended for up to 180 days; probation terminated.	7/13/2011 probation; 1/11/2017 probation terminated
[25]	Stephen Bernie	34200 Brookmeaed Court Solon, Ohio 44139	Cuyahoga	Guilty plea; license suspended then revoked.	4/2017 Guilty Plea; 5/10/2017 license suspension; 6/14/2017 license revoked
[26]	Syed Jawed Akhtar-Zaidi	34055 Solon Road, Suite 210 Solon, Ohio 44139	Cuyahoga	Indictment; license suspended.	8/27/2014 Indictment; 7/8/2015 license revoked
[27]	Thomas Craig	3270 Warrensville Center Road #305 Shaker Heights, Ohio 44122	Cuyahoga	Guilty plea; license revoked.	4/2018 Guilty Plea; 2/13/2019 license revoked
[28]	Toni Carman	Beachwood, Ohio	Cuyahoga	Guilty plea; license permanently surrendered.	4/29/2014 Guilty Plea; 7/10/2013 license surrender
[29]	William Balint Kerek	75 Arch Street, Suite 102 Akron, Ohio 44304	Summit	License suspended then reinstated.	1/13/2010 license suspended; 1/31/2011 license reinstated

Notes and Sources:

[1] AKRON_000368459, MCKPUB00000001, MCKPUB00000007, MCKPUB00005900, MCKPUB00028867.
[2] MCKPUB00000036, MCKPUB00024532, MCKPUB00028463, MCKPUB00028869.
[3] MCKPUB00028128, MCKPUB00028232, MCKPUB00028815, MCKPUB00028818, MCKPUB00028886, MCKPUB00028902, MCKPUB00028903, MCKPUB00028909.
[4] MCKPUB00024501, MCKPUB00028394.
[5] OSDB_MDL 1st Production_005794.
[6] MCKPUB00000047, MCKPUB00028770, MCKPUB00028780, MCKPUB00028888.
[7] MCKPUB00000065, MCKPUB00000068, MCKPUB00028690, MCKPUB00028817, MCKPUB00028874.
[8] MCKPUB00028370, MCKPUB00028859.
[9] MCKPUB00024548, MCKPUB00028314.
[10] MCKPUB00028255, MCKPUB00028872, OhioPharmMins_0000131, OhioPharmMins_0000139.
[11] OSDB_MDL 1st Production_007368.
[12] CLEVE_001486342, MCKPUB00000304, MCKPUB00000306, MCKPUB00028311, MCKPUB00028766, MCKPUB00028880.
[13] Also known as Stephen Gilreath. MCKPUB00000307, MCKPUB00000359, MCKPUB00028795, MCKPUB00028825, MCKPUB00028898,
[14] MCKPUB00028505, MCKPUB00028882.

Appendix B-1

[15]	MCKPUB00028661, MCKPUB00028876.
[16]	MCKPUB00028625, MCKPUB00028896.
[17]	MCKPUB00000367, MCKPUB00000383, MCKPUB00000386, MCKPUB00000388, MCKPUB00028130, MCKPUB00028890.
[18]	OSDB_MDL 1st Production_006030.
[19]	OSDB_MDL 1st Production_003148.
[20]	OSDB_MDL 1st Production_006838.
[21]	MCKPUB00024569, MCKPUB00028345.
[22]	CUYAH_000058274, MCKPUB00000393, MCKPUB00000395, MCKPUB00028773, MCKPUB00028782, MCKPUB00028892.
[23]	CUYAH_000054406, MCKPUB00000401, MCKPUB00000403, MCKPUB00000406, MCKPUB00028133, MCKPUB00028885.
[24]	MCKPUB00028732, MCKPUB00028758, MCKPUB00028765, MCKPUB00028865.
[25]	CUYAH_000071691, MCKPUB00000418, MCKPUB00000421, MCKPUB00000422, MCKPUB00000424, MCKPUB00000429, MCKPUB00028863.
[26]	MCKPUB00000431, MCKPUB00000434, MCKPUB00028900, SUMMIT_002053443.
[27]	MCKPUB00000509, MCKPUB00000513, MCKPUB00000514, MCKPUB00028792, MCKPUB00028894.
[28]	MCKPUB00028760, MCKPUB00028762, MCKPUB00028891.
[29]	MCKPUB00028136, MCKPUB00028878.

Appendix B-2

	Pharmacy	**Address of the Pharamcy**	**County**	**Outcome**	**Date**
[1]	Chesterfield Pharmacy	1799 E. 12th Street Cleveland, Ohio 44114	Cuyahoga	License revoked; pharmacy closed.	8/4/1999 License revocation

Notes and Sources:

[1] MCKPUB00000664, SUMMIT_002053140.

Appendix C
Abatement Program Categories Proposed by Plaintiffs' Experts

Proposed Program Category	Alexander	Keyes	Liebman	Lembke	Wexelblatt	Young
Medication Assisted Treatment	X	X	X	X	X	X
Other Treatment	X		X	X		
Criminal Justice Programs	X					X
Media Campaigns	X		X		X	
Naloxone Distribution	X	X	X	X		
Programs for Adolescents and Young Adults	X		X		X	
Medical Professional Education and Guidance	X		X	X	X	X
Pregnant Women/Neonatal Care and Treatment	X		X		X	X
Programs for Foster Care / Protective Services	X					X
Drug Disposal and Needle Exchange Programs	X		X	X		
Surveillance	X		X			
Fentanyl Testing	X	X				
Prescription Drug Monitoring Programs	X					
Research	X					
Law Enforcement Programs	X		X			

Notes and Sources:
Keyes Report, Sections C and F; Alexander Report, ¶¶ 40-181; Liebman Report, Sections VI and VII; Expert Report, Anna Lembke, M.D., pp. 89-97; Wexelblatt Report, Sections III and IV; Young Report, pp. 26-35.

CRA Charles River Associates

Exhibit I-1

Gregory K. Bell
Group Vice President

PhD, Business Economics
Harvard Graduate School of Arts and Sciences/
Harvard Graduate School of Business Administration

MBA, Harvard Graduate School
of Business Administration

BA, Simon Fraser University

Dr. Gregory K. Bell leads CRA's global Life Sciences Practice. As an expert witness, he frequently testifies on damages in intellectual property, finance, and antitrust litigation in courts and arbitration proceedings in North America, Europe, Asia, and Australia. Dr. Bell's business consulting engagements focus on the economics of business strategy, working with firms to develop sustainable competitive advantages in specific product markets. He has led and consulted to numerous projects concerning game theory and competitive strategy, global launch strategy, product pricing and positioning, capital budgeting and real options, and cost-benefit analyses.

Experience

Business

1992–Present *Group Vice President*, Charles River Associates, Boston, MA

- Dr. Bell has held numerous positions at CRA. Currently, he is the group vice president responsible for the firm's global Life Sciences Practice and the Business Advisory Group.

1987 *Management Consultant*, Alliance Consulting Group, Boston, MA

- Dr. Bell designed a market research program for a consumer electronics client's new product development.

1986 *Associate*, Corporate Finance, Wood Gundy, Vancouver, Canada

- Dr. Bell participated in drafting the prospectus and in marketing the initial public offering of a sportswear manufacturer.

1982–1985 *Chartered Accountant*, Pannell Kerr Forster, Victoria, Canada

- Dr. Bell provided financial accounting, auditing, taxation, and related management consulting services, focusing on special projects involving accounting theory, financial forecasts, and business valuations.
- He also developed a course to prepare the national firm's articling students for the uniform final examination, an examination required to receive the designation of chartered accountant.
- Dr. Bell placed eighth in Canada on the 1983 uniform final examination and was named to national honor roll.

Academic

1991–1992 *Visiting Assistant Professor*, Economics Department, Northeastern University

- Dr. Bell was responsible for undergraduate courses in industrial organization, managerial economics, and principles of microeconomics.

1991–1992 *Lecturer*, Economics Department, Harvard University

- Dr. Bell developed the senior-level undergraduate course, "Economics of Business Strategy."

Section Leader, Economics Department, Harvard University

- Dr. Bell led sections in industrial organization.

1990–1991 *Research Associate*, Economics Department, Harvard University

- Dr. Bell conducted mergers and acquisitions analysis.

1982 *Research Assistant*, Economics Department, Simon Fraser University

- Dr. Bell performed capital markets analysis.

Publications

"Litigation in the Pharmaceutical and Medical Device Sector." With J. Greenblatt, B. Torregrossa. *Corporate Disputes*. pp. 2–10. April–June 2018.

"Disputes in the Healthcare and Life Sciences Industry." With G. Breen, J. Dressel, M. Frisby. *Corporate Disputes*. pp. 2–13. April–June 2016.

"Damages in Life Sciences Arbitration." With J.K. Ho, A. Tepperman. Chapter 23 in *Global Arbitration Review, The Guide to Damages in International Arbitration*, pp. 320–330. London: Law Business Research Ltd, 2016.

"Damages in the Pharmaceutical and Biotech Sector." With I. Cockburn, C. Zayid. *Corporate Disputes*. pp. 4–14. April–June 2015.

"Managing Product Liability in the Pharma & Healthcare Sector." With P. Wilkinson, C. Zayid, M. Parini. *Corporate Disputes*. pp. 5–15. January–March 2015.

"Pharma and biotech patent litigation." With D. Schüssler-Langeheine, D. Nemec. *Corporate Disputes.* pp. 4–13. April–June 2014.

"Managing Dispute Resolution Strategy and Process." With C. Duclercq, E. Bos. *Corporate Disputes.* pp. 3–14. July–September 2013.

"Corporate Livewire Round Table: Biotech and Pharmaceutical." *Corporate Livewire,* June 2013.

"10 Questions: Quantification of Damages in Commercial Disputes." *Financier Worldwide Limited*, pp. 2–4. June 2012.

"Expert Witnesses in Arbitration." With M. Hammes, A. Yanos, J. Bédard. *Corporate Disputes.* pp. 2–13, *Financier Worldwide Limited*, October 2012.

"Future Innovations and Structural Changes." *Future Pharmaceuticals*, 2006.

"Global Pricing Strategies for Pharmaceutical Product Launches." With P. Rankin and T. Wilsdon. Chapter 2 of *The Pharmaceutical Pricing Compendium*, pp. 13–23, Urch Publishing Ltd, 2003.

"Cost Implications of Low Molecular Weight Heparins as Prophylaxis Following Total Hip and Knee Replacement." With S. Goldhaber. *Vascular Medicine,* February 2001.

"Economic Outcomes Analysis of Implantable Cardioverter Defibrillators." With M. Stanton. *Circulation*, March 2000.

"Clinical Realities and Economic Considerations: Economics of Intrathecal Therapy." With Samuel J. Hassenbusch et al. *Journal of Pain and Symptom Management*, September 1997.

"Cost-Effectiveness Analysis of Spinal Cord Stimulation in Treatment of Failed Back Surgery Syndrome." With D. Kidd and R. North. *Journal of Pain and Symptom Management*, May 1997.

"Irreversible Investments and Volatile Markets: A Study of the Chemical Processing Industry." With J. Campa. *Review of Economics and Statistics*, February 1997.

"Volatile Exchange Rates and the Multinational Firm: Entry, Exit, and Capacity Options." In L. Trigeorgis (ed.), *Real Options in Capital Investment*. Westport, CT: Praeger, 1995, pp. 163–181.

"Innovation in Cardiac Imaging." With S. Finkelstein and K. Neels. *Medical Innovation at the Crossroads,* Volume 5. Washington, DC: Institute of Medicine, National Academy Press, 1995, pp. 125–154.

"Illustrative Case Problem." With D. Wright. Chapter 13 in Deloris R. Wright, *US Transfer Pricing Guide: Practice and Policy*. CCH, 1995.

"Irreversible Investments and Volatile Exchange Rates: Theory and Evidence." PhD Thesis, Harvard University, 1992.

Presentations

Expert report on behalf of Defendants in United Healthcare Services, Inc. v. Cephalon, Inc., et al. (April 2019). United States District Court for the Eastern District of Pennsylvania. Case No. 2:17-cv-00555-MSG.

"Complex Issues in Life Sciences Arbitration." Panelist at International Court of Arbitration (ICC) seminar International Arbitration of Life Sciences Disputes: Key Issues and Best Practices, Boston, MA, April 2019.

"Biobetters vs. Biosimilars: Opportunities, Threats & Strategic Implications." Keynote speaker at International Conference on Biobetters and Regulatory Affairs, Vancouver, British Columbia, Canada, June 2018.

"Reverse Payments." Panelist at Federal Bar Council on Continuing Legal Education (CLE),

New York, NY, October 2014.

"A Pros and Cons Analysis of Launching At Risk and Survey of New Developments in Seeking Injunctive Relief and Damages." Panelist at American Conference Institute's 8th Annual Paragraph IV Disputes, New York, NY, April 2014.

"The Master Class on Settling Paragraph IV Disputes: Drafting and Negotiating Strategies for Brand-Names and Generics – A Hands-On, Practical Approach in the Aftermath of *Actavis*." Panelist at American Conference Institute's 8th Annual Paragraph IV Disputes, New York, NY, April 2014.

"Economic Perspectives on the PMPRB's Price Review Regime." 9th Annual Forum on Pharma Patents, Canadian Institute, Toronto, Canada, November 2010.

"Prejudgment Interest." Swedish Arbitration Association, Stockholm, Sweden, September 2010.

"Risk-sharing Contracts: Strategic and Practical Perspectives." Forum, NextLevel Pharma, Philadelphia, PA, October 2009.

"Innovation Strategy & IP." Licensing Executive Society (LES) Mini-Plenary. Panel chair at LES International Conference and LES (USA and Canada) Spring Meeting, Chicago, IL, May 2008.

"Damages: Lost Profits, Consequential Damages, Damages for Non-Patented Items, Best Practices for the Use of Experts." Panel participant for The Fifth Annual Sedona Conference on Patent Litigation, Sedona, AZ, October 2004.

"Patent Damages: Engineering and Regulatory Work-Arounds." Calculating and Proving Patent Damages, Law Seminars International, Reston, Virginia, June 14, 2004.

"Pricing Strategy and the Product Line." Pricex 2003, Chicago, IL, June 11, 2002.

"Reasonable Royalties for Emerging Technologies." Chaired Panel for The Third Annual Sedona Conference on Patent Litigation, Sedona, AZ, November, 2002.

"Does Price Matter? Pricing, Game Theory, and the Economics of Business Strategy." Pricex 2002, Chicago, IL, April 30, 2002.

"eCommerce and Strategy for the Pharmaceuticals Industry." Chairman for The Canadian National e-Pharma Summit II, Toronto, Canada, June 26–27, 2001.

"Exports and Flexible Production Technologies in Volatile International Markets." 4th Annual Conference on Real Options, Cambridge, UK, July 7–8, 2000.

"The Valuation of Oil Drilling Rights: A Real Options Case Study." 2nd Annual Conference on Real Options, Chicago, IL, June 11–12, 1998.

"Prejudgment Interest." Conference: Charles River Associates' Economists' Perspectives on Antitrust Today—Session: Topics in Calculating Damages, Boston, MA, April 30, 1998.

"Designing Licenses that Maximize Client Profits." American Intellectual Property Law Association Spring Meeting, Minneapolis, MN, April 23, 1998.

"Economics of Therapy." Nonmalignant Pain Management Roundtable, Memphis, TN, January 9, 1997.

"How to Structure Risk-Sharing Contracts to Put Teeth in Disease Management." Congress on Health Outcomes and Accountability, Washington, DC, December 10–13, 1995.

Balancing Low and High Risk Projects." Institute for International Research, Portfolio Planning & Management Conference, Philadelphia, PA, October 23–25, 1995.

"Capitated Pricing for Pharmaceuticals." Medical Marketing Association National Meeting, Monterey, CA, June 1995.

"Evaluating the Cost-Effectiveness of Pharmaceuticals." Anti-Rheumatic Guidelines and International Society for Rheumatic Therapeutics, Scottsdale, AZ, May 1995.

"The Role of Pharmacoeconomics in the Drug Approval Process." Anti-Rheumatic Guidelines and International Society for Rheumatic Therapeutics, Scottsdale, AZ, May 1995.

"Compliance with Section 482." With D. Wright. Institute for International Research, Practical Approaches to Transfer Pricing conference, New Orleans, LA, February 22–23, 1995.

"XYZ Corporation: A Case Study in Transfer Pricing." With D. Wright. Institute for International Research, Practical Approaches to Transfer Pricing conference, New Orleans, LA, February 22–23, 1995.

"Medtronic's Spinal Cord Stimulation Systems: Reimbursement and Marketing Strategy." Sloan School, Massachusetts Institute of Technology, Cambridge, MA, June 1993.

"Exports and Production Technology under Volatile Exchange Rates." Stanford University, Stanford, CA, February 1992.

"Capacity and Volatile Exchange Rates: A Study of the Chemical Processing Industry." London Business School, London, United Kingdom, March 1991; University of Michigan, Ann Arbor, MI, March 1991; University of British Columbia, Vancouver, BC, February 1991; Kellogg School of Management, Northwestern University, Evanston, IL, January 1991.

Testimony

Expert reports on behalf of Defendant in *UMB Bank, N.A. v. Sanofi (April 2019)*. United States District Court for the Southern District of New York, Case No. 15 Civ. 8725 (GBD) (RWL).

Declaration on behalf of Defendant *In re Intuniv Antitrust Litigation v. Direct Purchaser* (February 2019). United States District Court for the District of Massachusetts, Civil Action No.: 16-cv-12653-ADB (Direct).

Expert reports on behalf of Plaintiff in *Fresenius Kabi USA, LLC v. Par Sterile Products, LLC, et al.* (January, April 2019). United States District Court for the District of New Jersey, Civil Action No. 2:16-cv-04544 (SDW) (LDW).

Expert reports and deposition on behalf of Plaintiffs in *Galderma Laboratories, L.P., et al. v. Teva Pharmaceuticals USA, Inc.* (January, March 2019). United States District Court for the District of Delaware, Civil Action No. 17-1783 (RGA).

Expert reports on behalf of Defendant and Counterclaimant in *The University of Texas M.D. Anderson Cancer Center, Board of Regents of the University of Texas System, and University of*

Houston v. Otsuka Pharmaceutical co., LTD. (July, August, October 2018). 419th Judicial District Court of Travis County, Texas. Cause No. D-1-GN-000827.

Expert report and deposition on behalf of Defendant and Counterclaimant in *The United States and The Administrators of the Tulane Educational Fund v. Cytogel Pharma, LLC.* (July, August 2018). United States District Court for the Eastern District of Louisiana, Civil Action No. 2:16-cv-13987.

"Panelist: Business of Healthcare Tutorial" (July 2018) In re National Prescription Opiate Litigation MDL 2804, Northern District of Ohio, Denver, Colorado.

Expert report on behalf of Claimant in *Merck Sharp & Dohme (I.A.) LLC v. The Republic of Ecuador* (June 2018, March 2019). In the Matter of an Ad Hoc Arbitration under the UNICTRAL Arbitration Rules. PCA Case No. 2012-10.

Expert reports, deposition and arbitration testimony on behalf of Claimant in *Summers Laboratories, Inc. v. Shionogi Inc.* (June, July 2018). American Arbitration Association, Case No. Reference No. 01-17-0004-4710.

Expert report on behalf of Plaintiffs in *Abbott Laboratories, et al. v. H&H Wholesale Services, Inc., et al.,* (May 2018). United States District Court, Eastern District of New York, Case No. 1:17-cv-03095-CBA-LB.

Expert report and deposition on behalf of Plaintiffs in *Roche Diagnostics Corp. et al. v. Binson's Hospital Supplies, Inc. et al.,* (May, September 2018). United States District Court, Southern District of Indiana, Indianapolis Division, Civil Action No. 1:17-cv-0949 TWP-DML.

Expert reports and hearing testimony on behalf of Defendant in *Fortis Advisors LLC v. Merz, Incorporated, et al.,* (April, October, November 2018). International Chamber of Commerce, International Court of Arbitration, Civil Action No. 22758/MK.

Expert reports, depositions, and trial testimony on behalf of Plaintiff in *Incyte Corporation v. Flexus Biosciences, Inc., et al.* (April, May, November 2018). Superior Court of the State of Delaware in and for New Castle County, Complex Commercial Litigation Division, Civil Action No. N15C-09-055 MMJ.

Expert report, deposition, and hearing testimony on behalf of Defendants in *Frank Castellano, et al. v. HEB Grocery Company, LP, et al.* (April, May, November 2018). 389th Judicial District Court of the Hidalgo County, Texas, Civil Action No. C-1166-16.

Expert report and deposition on behalf of Defendant in *Icahn School of Medicine at Mount Sinai v. Neurocrine Biosciences, Inc.* (March, April 2018). United States District Court for the Southern District of New York, Case No. 1:15-cv-09414-RWS.

Expert report and deposition on behalf of Plaintiff in *Depomed, Inc. v. Purdue Pharma L.P., et al.* (January, March 2018). United States District Court for the District of New Jersey, Civil Action No.: 3:13-00571-BRM-TJB.

Declaration and deposition on behalf of Defendant in *Robert Bratton, et al. v. The Hershey Company* (December 2017, January 2018). United States District Court for the Western District of Missouri, Civil Action No.: 2:16-cv-4322-C-NKL.

Expert report and deposition on behalf of Defendants in *Roche Diagnostics GmbH, et al. v. Enzo Biochem, Inc., et al.* (November 2017, March 2018). United States District Court for the Southern District of New York. Civil Action No. 04 CV 4046 (RJS).

Expert reports on behalf of Defendants in *The Family Federation for World Peace and Unification International, et al. v. Hyun Jin Moon (a/k/a Preston Moon), et al.* (October, November 2017). Superior Court of the District of Columbia, Civil Division, Civil Case No. 2011 CA 003721 B.

Expert report, deposition, and hearing testimony on behalf of Defendants in *BASF AGRO B.V. et al. v. Makhteshim Agan of North America, Inc., et al.* (September 2017, January, April 2018). United States District Court for the Middle District of North Carolina, Civil Action No. Civil Action No. 1:10-CV-00276-WO-LPA.

Expert report and deposition on behalf of Defendants in *Amgen, Inc., et al. v. Sandoz, Inc., et al.* (September, October 2017). United States District Court for the Northern District of California, Civil Action No. 3:14-cv-04741-RS and 3:16-cv-02581-RS.

Affidavit on behalf of Defendant in the matter of *Duncan McDonald v. Samsung Electronics Canada Inc.* (September 2017). Ontario Superior Court of Justice, Court File 2610/16 CP.

Expert report, deposition, and testimony on behalf of Plaintiffs in *Shire Orphan Therapies LLC, et al. v. Fresenius Kabi USA, LLC,* (August, October 2017, January 2018). United States District Court for the District of Delaware, Civil Action No. 1:15-cv-01102-GMS.

Expert report and trial testimony on behalf of Defendant Impax Laboratories, Inc. in *In Re Solodyn (Minocycline Hydrochloride) Antitrust Litigation* (June, September 2017). United States District Court for the District of Massachusetts, Civil Action No. 14-md-02503-DJC.

Expert report on behalf of Respondent in *Exelixis, Inc. v. Genentech, Inc.,* (May 2017). Judicial Arbitration and Mediation Services (JAMS), Reference No. 1100084603.

Expert report on behalf of Defendant in *In re: Celebrex (Celecoxib) Antitrust Litigation* (May 2017). United States District Court for the Eastern District of Virginia, Norfolk Division, Lead Case No. 2:14-cv-361.

Expert reports and deposition on behalf of Plaintiffs in *Abbott Laboratories, et al. v. Adelphia Supply USA, et al.* (May 2017, January, February 2018). United States District Court for the Eastern District of New York, Case No. 15-cv-5826 (CBA) (MDG).

Expert report, deposition and declaration on behalf of Defendant in *Amgen Inc., et al. v. Hospira, Inc.* (April, May, November 2017). United States District Court for the District of Delaware, Case No. 1:15-cv-00839-RGA.

Expert report and deposition on behalf of Defendant in *Phigenix, Inc. v. Genentech, Inc.* (June, April 2017). United States District Court for the Northern District of California, San Jose Division, Case No. 15-cv-01238-BLF.

Expert reports, deposition, and testimony on behalf of Plaintiff in *Church & Dwight Co., Inc. v. SPD Swiss Precision Diagnostics, GmbH* (March, April, May, August, September 2017). United States District Court for the Southern District of New York, Case No. 1:14cv585 (AJN).

Expert report and deposition on behalf of Defendants in *In re: Lidoderm Antitrust Litigation* (June, March 2017). United States District Court, Northern District of California, Case No. 14-md-02521-WHO.

Expert report, deposition, and trial testimony on behalf of Plaintiffs in *Momenta Pharmaceuticals, Inc., et al. v. Amphastar Pharmaceuticals, Inc., et al.* (January, March, July 2017). United States District Court for the District of Massachusetts, Case No. 1:11-cv-11681-NMG.

Expert report and deposition on behalf of Plaintiffs in *Cadence Pharmaceuticals, Inc. et al. v. Innopharma Licensing LLC, et al.* (November, December 2016). United States District Court for the District of Delaware, Civil Action No. 14-1225 (LPS) (CJB).

Expert reports, declaration and testimony on behalf of Claimant in *Nektar Therapeutics v. Allergan, Inc. and MAP Pharmaceuticals, Inc.*, (July, August 2016, January, May 2017). JAMS Arbitration No. 1100080769.

Expert report, deposition, and testimony on behalf of Plaintiff in *Kowa Company, Ltd. et al. v. Amneal Pharmaceuticals LLC, et al.* (July, November 2016, January 2017). United States District Court for the Southern District of New York, Civil Action Nos. 14-CV-2758 (PAC), 14-CV-2647 (PAC), 14-CV-2759 (PAC), 14-CV-2760 (PAC), 14-CV-5575 (PAC), 14-CV-7934 (PAC), 14-CV-3935 (PAC).

Expert reports and arbitration testimony on behalf of Plaintiffs in *Pernix Therapeutics Holdings, Inc. et al. v. Glaxo Group Limited, et al.*, (July, September, October 2016). International Chamber of Commerce. International Court of Arbitration No. 21285/RD.

Expert reports, deposition, and trial testimony on behalf of Plaintiff in *Teva Pharmaceutical Industries, et al. v. Dr. Reddy's Laboratories, et al.* (April, May, July, September, October 2016). United States District Court for the District of Delaware, Civil Action No. 14-1171-GMS (Consolidated).

Declaration and deposition on behalf of Acorda Therapeutics, Inc. in *Coalition for Affordable Drugs (Adroca) LLC v. Acorda Therapeutics, Inc.* (July, September 2016). United States Patent Trial and Appeal Board, IPR2015-01850, IPR2015-01853, IPR2015-01857, IPR2015-01858.

Deposition and hearing testimony on behalf of Barr Laboratories Inc., Hoechst Marion Roussel Inc., The Rugby Group Inc., and Watson Pharmaceuticals Inc. in *Cipro Cases I & II (*May, November 2016). Superior Court of the State of California, County of San Diego, JCCP Proceeding Nos. 4154 & 4220.

Expert report on behalf of Plaintiff in *Ferring International Center S.A. v. Solmedical S.A.S.* (April 2016). International Centre for Dispute Resolution, Case No. 01-15-0003-4195.

Expert reports, deposition, and trial testimony on behalf of Plaintiff in *Acorda Therapeutics, Inc., et al. v. Alkem Laboratories Ltd., et al.* (April, June, August, September 2016). United States District Court for the District of Delaware, Civil Action No. 14-882-LPS (Consolidated).

Expert reports and deposition on behalf of certain Defendant in *CelestialRx Investments, LLC v. Joseph J. Krivulka et al.* (February, July 2016). In the Court of Chancery of the State of Delaware, Civil Action No. 1173-VCG.

Expert report and deposition on behalf of defendant Bristol-Myers Squibb in *State of Wisconsin v. Abbott Laboratories, et al.* (October, November 2015). State of Wisconsin Circuit Court, Dane County, Branch 9, Case No. 04 CV 1709.

Expert reports and deposition on behalf of Plaintiffs in *Chiesi USA, Inc., et al. v. Sandoz Inc., et al.* (September, October, November 2015). United States District Court for the District of New Jersey, Civil Action No. 1:13-cv-05723-NLH-AMD.

Declaration, expert reports, and deposition on behalf of Defendant in *Monica Barba and Jonathan Reisman, et al. v. Shire U.S., Inc., et al.* (March 2014, August, September 2015). United States District Court for the Southern District of Florida, Miami-Dade Division, Case No. 1:13-cv-21158-CIV-LENARD/GOODMAN.

Expert reports on behalf of Plaintiffs in *Cornerstone Therapeutics Inc., et al. v. Exela Pharma Sciences, LLC, et al.* (July, September 2015). United States District Court for the District of Delaware, Civil Action No. 1:13-cv-01275-GMS.

Expert report and arbitration testimony on behalf of Defendant, Merus Labs International, Inc., in *LG Life Sciences, Ltd. v. Chiesi, USA, Inc. et al.*, (May, September 2015). International Chamber of Commerce. ICC Arbitration No. 20420/RD.

Declarations and arbitration testimony on behalf of Claimant in *Meda Pharmaceuticals, Inc. v. Apotex Inc., et al.* (May, September, December 2015). International Centre for Dispute Resolution of the American Arbitration Association, Case No. 01-14-0001-6315.

Expert reports on behalf of Defendant in *Leo Pharmaceutical Products Limited A/S vs. Sandoz BV* (May 2015, June 2016, August 2018). District Court of The Hague.

Expert reports, deposition, and trial testimony on behalf of Plaintiffs in *Revolution Retail Systems, LLC., et al. v. Sentinel Technologies, Inc., et al.* (May, June 2015). In the Court of Chancery of the State of Delaware, Civil Action No. 10605 – VCP.

Expert report on behalf of Defendants in *The University of Utah v. Max-Planck-Gesellschaft zur Förderung der Wissenschaften E.V., et al.,* (April 2015). United States District Court for the District of Massachusetts, Civil Action No. 1:11-cv-10484.

Expert report and deposition on behalf of Defendants in *United States of America ex rel. Susan Ruscher, et al. v. OmniCare, Inc., et al.,* (April, May 2015). United States District Court, Southern District of Texas Houston Division, Civil No. 08-3396.

Expert report and deposition on behalf of Plaintiffs in *Reckitt Benckiser Pharmaceuticals, et al. v. Watson Laboratories, et al.,* (April, June 2015). United States District Court for the District of Delaware, Case No. 13-cv-1674-RGA; 1:14-cv-0422-RGA.

Expert report on behalf of Defendants in *Allergan USA, Inc. et al. v. Medicis Aesthetics, Inc. et al.,* (March 2015). United States District Court for the Central District of California, Civil Action No. SACV13-01436 AG (JPRx).

Expert report on behalf of Defendants in *Warner Chilcott Company, LLC et al. v. Teva Pharmaceuticals USA, Inc. et al.* (March 2015). United States District Court for the District of New Jersey, Civil Action No. 11-6936 (SRC) (CLW).

Expert report and deposition on behalf of Plaintiffs in *Innovation Ventures, LLC, Living Essentials, LLC and International IP Holdings, LLC v. Ultimate One Distributing Corp., et al.* (February, March 2015). United States District Court for Eastern District of New York, Civil Action No. 1-12-cv-5354 (KAM) (RLM).

Expert report, deposition, and trial testimony on behalf of Plaintiff in *Endo Pharmaceuticals v. Impax Laboratories* (December 2014, February 2015, April 2015). United States District Court, Southern District of New York, Civil Action Nos. 12-cv-8060-TPG, 12-cv-8115-TPG, 12-cv-8317-TPG, 12-cv-8318-TPG, 12-cv-8985-TPG, 12-cv-9261-TPG, 13-cv-435-TPG, 13-cv-436-TPG, 13-cv-3284-TPG, 13-cv-3288-TPG, 13-cv-4343-TPG, 13-cv-8597-TPG.

Hearings as a court-appointed expert in the matter of *Arrow Generics Limited v. Teva Czech Industries s.r.o.* (December 2014). Vienna Commercial Court, Case No. 12 Cg 38/05s.

Expert report and deposition on behalf of Plaintiff in *Theravectys SA v. Immune Design Corp.* (November, December 2014). Court of Chancery of the State of Delaware, Civil Action No. 9950-VCN.

Expert report on behalf of Respondent in *Progenics Pharmaceuticals, Inc. v. Ono Pharmaceutical Co. Ltd.* (July 2014). International Centre for Dispute Resolution of the American Arbitration Association, Case No. 50 122 T 01005 13.

Expert reports and testimony on behalf of Claimant in *Paul Gremillion, et al. v. HealthEdge Investment Fund, L.P., et al.* (June, September 2014). American Arbitration Association, Atlanta, Georgia, Claim No. 30 193 Y 00199 12.

Expert report on behalf of Plaintiff in *Zogenix, Inc. v. State of Massachusetts* (June 2014). United States District Court of Massachusetts, Civil Action No. 14-11689-RWZ.

Expert reports and testimony on behalf of Defendants in *Sanofi K.K. v. Novartis Pharma K.K.*, (May, December 2014, February, April 2015). International Court of Arbitration of the International Chamber of Commerce, ICC Arbitration Case No. 19250/CYK.

Expert report and deposition on behalf of Plaintiffs in *Galderma Laboratories L.P., et al. v. Actavis Mid Atlantic LLC.* (April 2014). United States District Court for the Northern District of Texas, Dallas Division, Civil Action No. 3:12-cv-02038-K.

Expert report and deposition on behalf of Plaintiff in *Enzo Biochem, Inc. v. Affymetrix, Inc.* (March, April 2014). United States District Court, Southern District of New York, Civil Action No. 03-CV-5446 (JES).

Expert reports and deposition on behalf of Plaintiff in *Enzo Biochem, Inc. v. PerkinElmer, Inc.* (January 2014). United States District Court, Southern District of New York, Civil Action No. 03-cv-03817 (JES).

Expert report and deposition on behalf of Plaintiffs in *Cadence Pharmaceuticals, Inc. et al. v. Fresenius Kabi USA, LLC et al.* (January, March 2014). United States District Court for the Southern District of California, Civil Action No. 3:13-cv-00139.

Expert reports and Declaration on behalf of Defendant in *Leon Khasin et al. v. The Hershey Company.* (January, April, June 2014). United States District Court Northern District of California, Case No. 12-cv-01862 EJD.

Expert reports and deposition on behalf of Plaintiff in *GlaxoSmithKline LLC v. Genentech, Inc.* (October, December 2013, January 2014). United States District Court for the District of Delaware, Civil Action No. 10-799-GMS.

Declaration of behalf of Cadence Pharmaceuticals, Inc. and SCR Pharmatop regarding Reexamination of U.S. Patent No. 6,028,222 (November 2013) before United States Patent and Trademark Office.

Expert report and deposition on behalf of Defendants in *Cardionet, Inc. et al. v. Mednet Healthcare Technologies, Inc., et al.* (September, October 2013). United States District Court for the Eastern District of Pennsylvania, Case No. 12-CV-2517 (JS).

Expert reports and deposition on behalf of Defendants in *Nexium (Esomeprazole) Antitrust Litigation.* (September, November, December 2013). United States District Court for the District of Massachusetts, MDL No. 2409, Civil Action No. 1:12-md-2409.

Expert report and deposition on behalf of Plaintiffs in *Takeda Pharmaceutical Company Limited et al. v. Mylan Inc. et al.* (June, November, December 2013). United States District Court Southern District of New York, ECF Case, Civil Action No. 12-CIV-0024 (DLC).

Expert reports, deposition, and trial testimony on behalf of Plaintiffs in *Cadence Pharmaceuticals, Inc. and SCR Pharmatop v. Exela Pharma Sciences, LLC, et al.* (April, June, July 2013). United States District Court for the District of Delaware, Civil Action No. 11-733-LPS.

Expert reports, deposition, and testimony on behalf of Defendant in *Napo Pharmaceuticals, Inc. v. Salix Pharmaceuticals, Inc.* (March, April 2013, February 2014). Supreme Court of the State of New York, County of New York, Commercial Division, Index No. 651214/2011.

Expert report on behalf of Defendants in *Luis Lerma and Nick Pearson, et al, v. Schiff Nutrition International, Inc., et al.* (March 2013). United States District Court, Southern District of California, Case No.: 11-CV-1056-CAB(MDD).

Expert report and deposition on behalf of Defendants in *Dr. Reddy's Laboratories et al. v. MDS, Inc. et al*. (September 2012, January 2013). United States District Court of New Jersey, Civil Action 09-2398 (AET).

Expert report on behalf of Defendant in *ThyssenKrupp Companhia Siderugica do Atlantico v. CITIC Group* (July 2012), Arbitral Tribunal, ICC Case No. 17894/JRF/CA.

Expert reports, deposition, and trial testimony on behalf of Defendant in *Tyco Healthcare Group LP et al. v. Ethicon Endo-Surgery, Inc.* (March, April, June, July 2012). United States District Court for the District of Connecticut. Civil Action No. 3:10cv00060 (JBA).

Expert reports on behalf of Respondent in *Genentech, Inc. v. UCB Celltech* (March, April 2012). American Arbitration Association, Case No. 50 122 T 00051 11.

Expert reports and deposition on behalf of Defendants in *Astellas US LLC et al. v. Fougera Pharmaceuticals Inc. f/k/a Nycomed US Inc.* (February, April, May 2012). United States District Court, District of New Jersey, Civil Action No. 10-cv-5599 (WJM) (MF) consolidated with No. 10-cv-6326).

Expert reports and deposition on behalf of Defendant in *Impax Laboratories, Inc. v. Shire LLC et al*. (November, December 2011, January 2012). United States District Court, Southern District of New York, Case No. 1:10-CV-08386 (MGC).

Expert report and deposition on behalf of Defendant in *Rembrandt Vision Technologies, L.P. v. Johnson & Johnson Vision Care, Inc.,* (November 2011). United States District Court, Middle District of Florida, Jacksonville Division, Case No. 3:11-cv-0819-J-32-JRK.

Expert report, deposition, and hearing testimony on behalf of Defendants in *State of Louisiana v. Abbott Laboratories, Inc., et al.,* Suit No. 596164, consolidated with *State of Louisiana v. McKesson Corporation*, Suit No. 597634 (August, September 2011). 19th Judicial District Court, Parish of East Baton Rouge, State of Louisiana.

Expert reports, depositions, and testimony on behalf of the Generic Defendants in *King Drug Company of Florence, Inc., et al. v. Cephalon, Inc., et al.* (June, August 2011, December 2013, January, February 2014, June 2017). United States District Court for the Eastern District of Pennsylvania, Civil Action No. 06-cv-1797.

Expert report on behalf of Defendant in *Leo Pharma A/S and Leo Laboratories Limited v. Sandoz Limited* (April 2011). High Court of Justice, Chancery Division, Patents Court, HC 08 C00391.

Expert reports and arbitration testimony on behalf of Defendants in *Mitsubishi Tanabe Pharma Corporation (Japan) v. Centocor Ortho Biotech, Inc. (USA),* (January, March, October, November 2011, April, June 2012). International Court of Arbitration, Case No. 16048/VRO.

Expert reports and arbitration testimony on behalf of Defendant in *MDS (Canada) Inc. v. Atomic Energy of Canada Limited* (November 2010, April 2011, October 2011). Arbitration, Toronto, Canada.

Expert report and trial testimony on behalf of Bristol-Myers Squibb in *Commonwealth of Pennsylvania v. TAP Pharmaceutical Products, Inc., et al.* (August, September 2010). Commonwealth Court of Pennsylvania, No. 212 MD 2004.

Expert report and deposition on behalf of Plaintiffs in *King Pharmaceuticals, Inc., et al. v. Purdue Pharma L.P.*, (June, July 2010). United States District Court for the Western District of Virginia, Abingdon Division, Civil Action No. 1:08-CV-50-JPJ-PMS.

Declaration and deposition on behalf of Pfizer, Inc. *In Re Neurontin Antitrust Litigation* (May 2010, October 2010). United States District Court, District of New Jersey, MDL Docket No. 1479 (FSH), Master Docket No. 02-CV-1390.

Expert report and deposition on behalf of Plaintiffs in *Takeda Pharmaceutical Company Limited et al. v. Teva Pharmaceutical Industries, Ltd., et al.* (May 2010, June 2010). United States District Court Southern District of New York, Civil Action No. 4655.

Expert report and deposition on behalf of Plaintiffs in *Takeda Chemical Industries, Ltd., et al. v. Ranbaxy Pharmaceuticals, et al.* (March, June 2010). United States District Court Southern District of New York, Civil Action Nos. 03 CIV 8250 (DLC), 03 CIV 8253 (DLC), and 03 CIV 8254 (DLC).

Expert reports on behalf of Plaintiffs in *SmithKline Beecham Corporation, et al. v. Apotex Corporation, et al.* (December 2009, January 2010). United States District Court for the Eastern District of Pennsylvania, Civil Action No. 99-CV-4304.

Expert report, deposition, and trial testimony on behalf of Plaintiffs/Counterdefendants in *Underwriters at Lloyd's London v. Abbott Laboratories* (December 2009, February 2010, February 2013), Circuit Court of Cook County, Illinois County Department, Chancery Division, No. 03 CH 9307.

Expert report, deposition, and trial testimony on behalf of Plaintiffs in *Mitsubishi Chemical Corporation, et al. v. Barr Laboratories, et al.* (May 2009, July 2009, February 2010). United States District Court for the Southern District of New York, Civil Action No. 07 CV 11614.

Affidavits and hearing testimony on behalf of Respondent in the matter of *ratiopharm Inc. and the Medicine "ratio-salbutamol HFA"* (April, December 2009, April 2010). Patented Medicine Prices Review Board, Ottawa, Canada.

Declaration on behalf of Defendants regarding *State of Hawaii v. Abbott Laboratories Inc. et al.* (March 2009). In the Circuit Court of the First Circuit, State of Hawaii, Civil Action No. 06-1-0720-04 EEH.

Expert reports and arbitration testimony on behalf of Defendant in *Monsanto Company and Monsanto International Sàrl v. Sandoz Gmbh* (March, December 2009, October 2010), Arbitral Tribunal, ICC Case No. 15117/JHN.

Expert report and deposition on behalf of Defendant in *Invesco Institutional (N.A.), Inc. v. Deutsche Investment Management Americas* (February, April 2009). Supreme Court of the State of New York, County of New York, Index No. 650154/2007, Part 39.

Declaration on behalf of Defendant in *AstraZeneca v. Ivax Pharmaceuticals, Inc.* (November 2008). United States District Court for the District of New Jersey, Civil Action No. 05-5142 (RMB)(AMD).

Declarations on behalf of Defendant in *Eli Lilly and Company v. Teva Pharmaceuticals USA, Inc.* (October 2008, February 2009). United States District Court, for the Southern District of Indiana, District of Columbia, Case Number 1:06-cv-1017-SEB-JMS.

Expert report and deposition on behalf of Plaintiff in *Intervet Inc. v. Merial Limited and Merial SAS* (August, October 2008). United States District Court, for the District of Columbia, Civil Action No. 1:06-cv-00658 (HHK-JMF).

Expert report and deposition on behalf of Defendants in *The Boston Company Asset Management, LLC v. Remi Browne, et al.* (May, July 2008). Commonwealth of Massachusetts, Superior Court Department of the Trial Court, Suffolk, ss., Civil Action No. 07-3656 BLS2.

Declaration on behalf of Defendants in *Gregory Clark and Linda Measheу, et al. v. Pfizer, Inc. et al.* (May 2008). Court of Common Pleas of Philadelphia County, First Judicial District of Pennsylvania, Civil Trial Division, June TERM, 2004/No. 1819.

Expert report and deposition on behalf of Defendant in *Synthes (USA) v. Smith & Nephew* (May, August 2008). United States District Court, Eastern District of Pennsylvania, Civil Action No. 03CV0084.

Declarations on behalf of Pfizer, Inc. *In Re Neurontin Marketing, Sales Practices, and Products Liabilities* (March, December 2008). United States District Court, District of Massachusetts, MDL Docket No. 1629, Master File No. 04-10981.

Expert report, deposition, and trial testimony on behalf of Plaintiffs in *Aventis Pharmaceuticals Inc. and sanofi-aventis US LLC v. Barr Laboratories, Inc.* (January, February, May 2008). United States District Court for the District of Delaware, Civil Action No. 06-286 (GMS).

Expert report on behalf of Respondent in *Amgen Inc. v. F. Hoffmann-La Roche Ltd* (January 2008). Arbitral Tribunal, ICC No. 14826.

Expert report and trial testimony on behalf of Plaintiff in *Church & Dwight Co., Inc. v. Abbott Laboratories* (August, October 2007, January, February 2008). United States District Court for the District of New Jersey, Civil Action No. 05 CV 2142 (GEB).

Affidavit and deposition on behalf of Defendants in the matter of *State of Wisconsin v. Amgen Inc., et al.* (July, August 2007). State of Wisconsin Circuit Court, Dane County, Case No. 04 CV 1709.

Expert report and deposition on behalf of Barr Pharmaceuticals, Inc., in *Meijer, Inc., et al. v. Warner Chilcott Holdings Company III, LTD., et al.* (June, August 2007). United States District Court for the District of Columbia, Civil Action Nos: 05-2195 (CKK), 06-00494 (CKK), and 06-00795 (CKK).

Declaration on behalf of Teva Pharmaceuticals in the matter of *Abbott Laboratories et al. v. Sandoz, Inc. et al.* (April 2007). United States District Court for the Northern District of Illinois Eastern Division, No. 07-CV-1721.

Expert reports, deposition, and trial testimony on behalf of Plaintiff in *Enzo Biochem, Inc. v. Applera Corp. et al.* (February, March, April 2007, October, December 2012). United States District Court, District of Connecticut, Civil Action No. 3-04-CV-929 (JBA).

Merits report and declarations on behalf of Defendants regarding the states of Montana (CV-02-09-H-DWM) and Nevada (02-CV-00260-ECR) in *Pharmaceutical Industry Average Wholesale Price Litigation* (February, May 2007). United States District Court, District of Massachusetts, MDL No. 1456, Civil Action No. 01-CV-12257-PBS.

Affidavit, expert report, and hearing testimony on behalf of Respondent in the matter of *Warren Lammert, et al.* (January, September, November 2007). United States of America, Securities and Exchange Commission, Administrative Proceeding, File No. 3-12386.

Affidavit and hearing testimony on behalf of Respondent in the matter of *Teva Neuroscience G.P.-S.E.N.C. and the medicine "Copaxone"* (January, February 2007). Patented Medicine Prices Review Board, Ottawa, Canada.

Expert reports on behalf of Barr Pharmaceuticals, Inc., et al. in *Federal Trade Commission and State of Colorado v. Warner Chilcott Holdings Company III, LTD., et al.* (December 2006, January 2007). United States District Court for the District of Columbia, Civil Action Nos: 05-2179 (CKK) and 05-2182 (CKK).

Expert report and deposition on behalf of MedImmune, Inc. in *Biosynexus, Inc. v. Glaxo Group Limited and MedImmune, Inc.* (November 2006, January 2007). Supreme Court of the State of New York, County of New York, Index No. 604485/05.

Expert report on behalf of Plaintiffs in *TAP Pharmaceutical Products, Inc., et al. v. Atrix Laboratories, Inc., et al.* (October and November 2006). United States District Court, Northern District of Illinois, Case No. 03-C-7822.

Affidavit on behalf of Defendants in *State of Alabama v. Abbott Laboratories, Inc., et al.* (September 2006). Circuit Court of Montgomery County, Alabama, Civil Action No. 2005-219.

Expert report on behalf of Plaintiffs in *GlaxoSmithKline Holdings (Americas) Inc. et al. v. Commissioner of Internal Revenue* (August 2006). United States Tax Court, Docket Nos. 5750-04 and 6959-05.

Expert report and arbitration testimony on behalf of Respondent in *Roche Diagnostics GmbH v. SmithKline Beecham Pharma GmbH & Co. KG* (July, November 2006). ZCC Arbitration No. 516.

Affidavit on behalf of Pharmacia Corporation in *State of Connecticut v. Pharmacia Corporation* (May 2006). Superior Court of Connecticut, Complex Litigation Docket at Tolland, Docket No. X07-CV-03 0083297S.

Affidavit on behalf of Defendants in *State of Connecticut v. Roxanne Laboratories, et al.* (May 2006). Superior Court of Connecticut, Complex Litigation Docket at Tolland, Docket No. TTD-X07-CV-03 0083296S.

Expert report and deposition on behalf of Defendant in *Affinion Loyalty Group, Inc. v. Maritz, Inc.* (April 2006). United States District Court, District of Delaware, Civil Action No. 04-360.

Expert report, affidavit, and trial testimony on behalf of Bristol-Myers Squibb in *Pharmaceutical Industry Average Wholesale Price Litigation* (March, November, December 2006). United States District Court, District of Massachusetts, Civil Action No. 01-CV-12257-PBS.

Expert report and deposition on behalf of Plaintiff in *LoJack Corporation v. Clare, Inc.* (December 2005, January 2006, March 2006). Commonwealth of Massachusetts Superior Court, Civil Action No. 03-00627.

Expert report and deposition on behalf of Defendant in PHT *Corporation v. Invivodata, Inc.* (November, December 2005). United States District Court of Delaware, C.V. No. 04-60 GMS.

Expert report and deposition on behalf of Defendant in *PHT Corporation v. CRF, Incorporated* (November, December 2005). United States District Court of Delaware, C.V. No. 04-61 GMS.

Expert reports and trial testimony on behalf of Defendant in *Her Majesty The Queen v. GlaxoSmithKline* (October 2005, January, April 2006). Tax Court of Canada, Court File No. 98-712(IT)G.

Expert report and deposition on behalf of Plaintiffs in *IVPCare, Inc. v. Harvard Pilgrim Health Care, Inc.* (October, November 2005). Superior Court Department of the Trial Court, Commonwealth of Massachusetts, Civil Action No. 03-5058-BLS.

Expert reports and deposition on behalf of Plaintiffs in *Pharmacia & Upjohn Company, LLC v. Sicor Inc., et al.* (September 2005, February, April, October 2006). US District Court of Delaware, Civil Action No. 04-833 (KAJ).

Expert reports and deposition on behalf of Defendant in *Applera Corporation et al. v. Wyeth, Inc.* (August, September, October 2005). Circuit Court for Montgomery County, Maryland, Civil Action No. 242761.

Expert reports and deposition on behalf of Defendant Medco Health Solutions, Inc., et al. in *US Government v. Merck-Medco et al.* (August, September, October, November 2005). United States District Court, Eastern District of Pennsylvania, No. 00-CV-737.

Expert reports and deposition on behalf of Defendant FMC Corporation in *Microcrystalline Cellulose Antitrust Litigation* (April, May, June 2005). United States District Court, Eastern District of Pennsylvania, Master File No. 01-CV-111 (O'Neill, J.) MDL No. 1402.

Expert report on behalf of Defendants in *Robert J. Swanston v. TAP Pharmaceutical Products, Inc., et al.* (February 2005). Superior Court of the State of Arizona in and for the County of Maricopa, Cause No. CV2002-004988.

Expert reports on behalf of Claimant in *Joint Services International, B.V. v. O'Neill, Inc.* (January, April 2005). London Court of International Arbitration (LCIA), LCIA Arbitration No. 3513.

Expert report and deposition on behalf of Defendants in *RoseMarie Ryan-House, et al. v. GlaxoSmithKline, et al.* (December 2004). United States District Court, Eastern Division of Virginia, Civil Action No. 2:02cv442.

Expert reports, tutorial, affidavit, and testimony on behalf of Fast Track Defendants in *Pharmaceutical Industry Average Wholesale Price Litigation* (December 2004 and March, November, December 2006). United States District Court, District of Massachusetts, Civil Action No. 01-CV-12257-PBS.

Expert report and deposition on behalf of Plaintiff in *Yangtze Optical Fibre and Cable Company LTD. v. Lucent Technologies Inc.* (November 2004, March 2005). United States District Court, District of Massachusetts, Civil Action No. 03CV11413EFH.

Expert report and deposition on behalf of Defendants in *Medtronic Vascular, Inc. v. Boston Scientific Corporation, et al.* (July, August 2004). United States District Court, District of Delaware, Civil Action No. 98-478 SLR.

Expert report and deposition on behalf of Mylan Laboratories, Inc., et al. in *Lorazepam & Clorazepate Antitrust Litigation* (May, June 2004). United States District Court, District of Columbia, MDL No. 1290 (TFH).

Affidavit on behalf of Novopharm Limited in *Pfizer Canada et al. v. The Minister of Health and Novopharm Limited* (May 2004). Federal Court, Court File No. T-2448-03.

Expert report and deposition on behalf of Bayer AG and Bayer Corporation in *Ciprofloxacin Hydrochloride Antitrust Litigation* (April, May 2004). United States District Court, Eastern District of New York, Master File No. 1:00-MD-1383.

Affidavit and testimony on behalf of Novopharm Limited in *Merck & Co et al. v. The Minister of Health and Novopharm Limited* (April, August 2004). Federal Court, Court File No. T-1627-03.

Expert report and deposition on behalf of Defendants in *Corning Incorporated et al. v. SRU BioSystems et al.* (April, May 2004). United States District Court, District of Delaware, Civil Action No. 03-633-JJF.

Expert reports and arbitration testimony on behalf of Respondent in *Roche Diagnostics GmbH v. SmithKline Beecham (Cork) Ltd* (January, April, July 2004). ZCC Arbitration No. 362.

Expert report and arbitration testimony on behalf of Claimant in *Hans-Werner Hector v. The Bank of America Corporation et al.* (January, April 2004). American Arbitration Association.

Expert report on behalf of Plaintiff in *Enzo Biochem, Inc. v. Gen-Probe, Inc. et al.* (December 2003). United States District Court, Southern District of New York, Civil Action No. 99-4548 (AKH).

Expert report on behalf of Defendants in *Truitt Enterprises et al. v. Union Security Life Insurance Company et al.* (November 2003). United States District Court, District of Maryland (Northern Division), Civil Action No. 03-1422.

Expert report and deposition on behalf of Plaintiffs in *DataSafe, Inc. et al. v. Federal Express Corporation et al.* (August 2003, January 2004). Commonwealth of Massachusetts, Superior Court Department, Civil Action No. 01-2590.

Expert report on behalf of Plaintiff in *SmithKline Beecham Animal Health Inc. v. Her Majesty The Queen* (July 2003). The Court of Queen's Bench, File No. 95-1077 (IT) G.

Expert report on behalf of Bayer Corporation in *Cipro Cases I & II* (June 2003). Superior Court of the State of California, County of San Diego, JCCP. Proceeding Nos. 4154 and 4220.

Expert reports and deposition on behalf of Defendants in *Johnson Matthey Inc. v. Research Corporation, et al.* (March, April 2003). United States District Court, Southern District of New York, Case No. 01-CV-8115 (MBM).

Expert report and deposition on behalf of Defendants in *Anne Cunningham, et al. v. Bayer AG, et al.* (March, April 2003). Supreme Court of the State of New York, County of New York, Index No. 603820-00.

Expert report and deposition on behalf of Defendants in *Tyco Adhesives LP v. Olympian Tape Sales, Inc. et al.* (August, October 2002). United States District Court, District of Massachusetts, Civil Action No. 00-11965-NG.

Expert reports, deposition, and trial testimony on behalf of Plaintiff in *Star Scientific v. R.J. Reynolds Tobacco Company* (January, March 2003, October 2004, March 2009, June 2009). United States District Court for the District of Maryland, Southern Division, Case No. AW 01-CV-1504/AW 02-CV-2504 and Civil Action No. MJG-01-CV-1504.

Expert report on behalf of Defendant in *Cook Incorporated v. Boston Scientific Corporation* (August 2002). United States District Court for the Northern District of Illinois, Eastern Division, Civil Action No. 01-CV-9479.

Deposition and trial testimony on behalf of Defendants in *Engelhard Corporation v. Research Corporation, et al.* (July, October 2002). Supreme Court of the State of New York, County of New York, Index No. 601847/98.

Expert report and arbitration testimony on behalf of Plaintiffs in *Biovail Laboratories Incorporated v. Mylan Pharmaceuticals, Inc.* (July 2002, January 2003). American Arbitration Association, Case No. 50T13329601.

Expert reports and deposition on behalf of Plaintiffs in *Novartis Consumer Health, Inc. v. Elan Transdermal Technologies et al.* (June, July, August 2002). United States District Court Southern District of Florida, Miami Division, Civil Action No. 01-1120-CIV-MOORE.

Expert report on behalf of Defendants in *Frederick F. Buechel, MD and Michael J. Pappas, PhD v. John N. Bain, John G. Gilfillan, III et al.* (March 2002). Supreme Court of the State of New York County of New York, No. 106963/95.

Expert reports and deposition on behalf of Defendants in *National Rural Electric Cooperative Association et al. v. Breen Capital Services Corporation et al.* (February 2002, October 2004). United States District Court of New Jersey, Civil Action No. 2:00cv00722.

Expert report on behalf of Plaintiff in *Aesculap AG & Co. et al. v. Walter Lorenz Surgical, Inc.* (November 2001). United States District Court for Northern District of California, No. C00-02394-MJJ.

Certification on behalf of Defendants in *Louise Garretson et al. v. CSFBTLC Trust II et al.* (October 2001). United States Superior Court for the District of New Jersey, No. HUD-L-3117-00.

Expert report and arbitration testimony on behalf of Respondent in *N.M.T. Medical, Inc. v. C.R. Bard, Inc.* (April 2001). American Arbitration Association, AAA Case No. 11 199 00973 00.

Expert report and arbitration testimony on behalf of Claimant in *Boston Scientific Corp. et al. v. Medtronic AVE, Inc.* (March and April 2001). American Arbitration Association, AAA File No. 50 T 133 00307 00.

Expert report and deposition on behalf of Defendants in *DuPont Pharmaceuticals, et al. v. Molecular Biosystems, Inc., et al.* (January and February 2001). United States District Court for the District of Delaware, Civ. No. 99-273 (JJF).

Expert reports on behalf of Defendant in *Sawgrass Systems, Inc., v. BASF Corporation* (December 2000, January 2001). United States District Court for the District of South Carolina, Civ. 2:98-3574-11 and 2:99-912-1.

Expert reports and deposition on behalf of Plaintiffs in *Apothecon, Inc., et al. v. Barr Laboratories, Inc., et al.* (November 2000, April 2001, June 2005, January, February, March 2006). United States District Court for the District of Southern New York, No. 98 Civ. 0861 (RWS) and No. 99 Civ. 3687 (RWS).

Expert report on behalf of Plaintiff in *Wold Trona Company, Inc. v. SNC-Lavalin America, Inc., et al.* (October 2000). United States District Court for the District of Wyoming, Civ. No. 00CV-1008B.

Expert reports, deposition, and trial testimony on behalf of SciMed Life Systems, Inc., and Boston Scientific Corporation in *Cordis Corporation v. Advanced Cardiovascular Systems, Inc., et al.* (August, November, and December 2000). United States District Court for the District of Delaware, Civ. No. 97-550-SLR.

Expert reports and deposition on behalf of Defendant in *Cordis Corporation v. Boston Scientific Corporation and SciMed Life Systems Inc.* (August and November 2000). United States District Court for the District of Delaware, Civ. No. 98-197-SLR.

Expert report and deposition on behalf of Defendants in *Advanced Cardiovascular Systems, Inc. and Guidant Sales Corporation v. SciMed Life Systems, Inc. and Boston Scientific Corporation* (November and December 1999). United States District Court for the District of Indiana, IP 98-1108-C-H/G.

Affidavit on behalf of Defendants in *Apotex Fermentation Inc. and Apotex Inc. v. Novopharm Ltd. et al.* (October 1999). The Court of Queen's Bench, File No. CI 93-01-73733.

Expert report and deposition on behalf of Bausch & Lomb, Inc., in *Disposable Contact Lens Antitrust Litigation* (July 1999, August 1999). United States District Court for the District of Florida, 94-MDL 1030-J-20A.

Expert reports and trial testimony on behalf of Defendants in *Unilever PLC et al. v. Procter & Gamble Inc. et al.* (January 1999, December 1999). Federal Court of Canada, T-2534-85.

Expert report for mediation submitted on behalf of Breen Capital in *City of Jersey City v. Breen Capital* (December 1998). Superior Court of New Jersey, C-57-98.

Expert reports, deposition, and trial testimony on behalf of Plaintiff in *Braintree Laboratories, Inc., v. Nephro-Tech, Inc., et al.* (November 1998, September 1999, June 1999, October 1999). United States District Court for the District of Kansas, 96-CV-2459.

Expert report on behalf of Defendant in *Ethicon Inc. and Johnson & Johnson Consumer Products Inc. v. Artegraft, Inc.* (September 1998). American Arbitration Association, File 18-199-00136-96.

Expert report and deposition on behalf of Defendant in *The Dow Chemical Corporation v. Astro-Valcour, Inc.* (June 1998, July 1998). United States District Court for the Northern District of New York, 95-CV-1357.

Expert reports and deposition on behalf of Defendant in *Emory University v. Glaxo Wellcome* (February 1998, August 1998, September 1998). United States District Court for the Northern District of Georgia, 96-CV-1754.

Expert reports and deposition on behalf of Defendant in *Emory University v. Glaxo Wellcome* (November 1997, March 1998, April 1998). United States District Court for the Northern District of Georgia, 96-CV-1868.

Expert reports on behalf of Defendant in *Johnson & Johnson v. American Home Products* (June 1996). United States District Court for the Eastern District of Pennsylvania, 94-CV-1388.

Trial testimony on behalf of Defendants in *Genentech, Inc. v. Novo Nordisk A/S et al.* (May 1996). United States District Court for the Southern District of New York, 96-CV-1755.

Consulting projects

Antibiotics

- Pricing and managed care strategy to support launch of quinolone. Market research with managed care and physicians.
- Evaluation of European reimbursement environment for launch of quinolone.
- Managed care strategy for quinolone. Market research with managed care.
- Pricing and managed care strategy to support launch of ketolide. Market research with managed care and physicians.

Blood products

- Cost-effectiveness study for anti-clotting product.
- Strategy for anti-anemia product as it faces competing entry. Market research with managed care, physicians, hospitals, and patients. Address new Medicare policies regarding ASP and CAP.
- Pricing and managed care strategy for anti-clotting product facing competing entry. Market research with managed care and physicians.
- Reimbursement issues for clotting factor.
- Assessment of tender contagion issues in a global market.
- Assessment of global pricing policy,

Cardiovascular products

- Managed care contracting strategy for statins. Market research with physicians.
- Capitated pricing strategy for statins.
- Pricing and managed care strategy to support global launch of a new class of cardiovascular products for the treatment of hypertension and heart failure. Markets include US, Canada, and Europe. Market research with managed care and physicians.
- Managed care strategy for anti-platelet product.
- Opportunity assessment for cardiac rehabilitation program.
- Managed care simulation for novel anti-coagulant.
- Strategic option assessment and pricing and managed care strategy to support US launch of new hypercholesterolemia product. Market research with payers and physicians.

CNS products

- Pricing and managed care strategy to support launch of prescription pain product. Market research with managed care, physicians, and patients.
- Managed care strategy to support dissolving formulation of anti-psychotic.

- Strategy review for Alzheimer's product.
- Managed care strategy for insomnia product facing competitive entry. Market research with managed care.
- Managed care strategy and sales force training to support launch of depot formulation of anti-psychotic. Market research with managed care.
- Managed care strategy to protect opioid analgesic business as product goes generic. Market research with managed care and physicians.
- Managed care strategy to support franchise products for the prevention and treatment of migraines.
- Managed care strategy to support anti-psychotic franchise confronting competing entry, generic penetration, and preparation for launch of second-generation product. Market research with managed care.
- Pricing and managed care strategy to support the launch of a long-acting opioid. Market research with managed care, physicians, and patients.
- Global portfolio strategy, product positioning, pricing, and competitor response issues for multiple sclerosis franchise. Markets include US, Europe, and Canada. Market research with payers and KOLs.
- Opportunity assessment for new patch product for Alzheimer's disease. Markets include US and Europe. Market research with managed care, physicians, and care-givers.
- Pricing strategy for infused multiple sclerosis product. Market research with managed care, physicians, and office managers.
- Managed care strategy to support the launch of a new addiction treatment product.
- Competitor response strategy for multiple sclerosis franchise. Market research with managed care, physicians, and office managers.

Dermatology

- Pricing and managed care strategy to support the launch of a prescription facial hair removal product.
- Launch strategy for a psoriasis treatment. Market research with managed care and physicians.
- Comprehensive review of pricing and contracting strategy across all channels. Market research with payers.
- Development of at-risk contracting strategy.

Endocrinology

- Managed care strategy to support the launch of extended-release and combination diabetes products. Market research with managed care.
- Pricing and managed care strategy to support launch of menopause product. Market research with managed care and physicians.

- Pricing and managed care strategy to support launch of an orphan drug product for Gaucher's disease. Market research with managed care, physicians, and patients.
- Advise on global pricing for growth hormone anticipating competitive entry.
- Evaluation of managed care and Medicaid contracting strategy and performance for a diabetes portfolio.
- Global pricing and product positioning strategy for blood glucose monitoring systems.
- Opportunity assessment regarding natural and analog insulins.

Gastro-intestinal products

- Cost-effectiveness study of GI impact of NSAIDs.
- Capitated pricing strategy for H2 antagonists.
- Managed care strategy and sales force training to support the launch of PPI. Market research with managed care and physicians.
- Capitated pricing strategy for PPI.
- Impact of launch of competing PPI. Market research with managed care and physicians.
- Impact of PPI going generic.

Nutritionals

- Value of government (WIC) contracts in the infant formula business. Study covered all aspects of consumer behavior and all aspects of manufacturing and distribution, including shelf facings at drug stores, mass merchandisers, and super-markets. Market research focused on purchasing and consumption behavior.
- Advise on bid pricing strategy for government contracts.
- Advise on likely exit strategy of competitor.
- Optimal size for ethical sales force, calling on hospitals and pediatricians.
- Design program for private-sector leadership to combat low-birth weight.
- Assess opportunity for new manufacturing facility and packaging options.
- Advise on likely entry strategy of potential competitor.
- Pricing strategy across product line. Market research with consumers.
- Evaluate opportunity to purchase pumps and plastics business for enteral feeding.
- Assess value of a patient/consumer regarding awareness/trial/usage. Market research involving patients.
- Assess value of hospital contracts for feeding systems in Canada. Market research involving patients and hospitals.

Oncology

- Strategy for second-generation oncolytic as predecessor product goes generic. Market research with physicians and hospitals.
- Strategy for oncolytic as it goes generic. Market research with physicians and hospitals.
- Pricing and managed care strategy to support the launch of a second-generation oncolytic. Market research with physicians and hospitals.
- Diagnostic strategy for breast cancer. Market research with physicians.
- Contracting strategy alternatives to support the launch of an oncolytic. Market research with physicians.
- Contracting strategy alternatives for oral oncolytics. Market research with payers and physicians.

Ophthalmology

- Develop pricing and contracting strategies, including new indication opportunity and assessment of competitor response. Market research with payers and physicians.
- Assess opportunity with and potential strategies for collaborating with GPOs to build category opportunity and gain product share.

Respiratory

- Distribution strategy for a specialty pharmacy asthma product.
- European launch strategy for COPD product.
- Assess opportunity for contracting strategy and consider ASP exposure. Interviews with payers and pharmacies.

Rheumatology

- Managed care strategy to support the launch of a new indication.
- Global opportunity assessment for a pipeline product. Particular focus on payer receptivity in US, Canada, France, and UK.
- Competitive strategy analysis for rheumatoid arthritis treatment. Market research with physicians, managed care, and specialty pharmacy.
- Portfolio positioning and contracting strategy.
- Hospital strategy for an infused anti-TNF.
- Launch strategy for an anti-TNF. Market research with physicians, patients, and managed care.
- Contracting strategy for rheumatology product. Market research with managed care and physicians.

- Assessment of biosimilar opportunity and strategies for response. Market research with payers, hospitals, and physicians.
- Comprehensive review of pricing and contracting strategy across all channels. Market research with payers.
- Development of at-risk contracting strategy.

Urology

- Managed care strategy to support incontinence product. Market research with managed care, physicians, and patients.
- Managed care strategy to support the launch of a product for premature ejaculation. Market research with managed care, physicians, and patients.
- Pricing and managed care strategy to support the launch of a product to treat enlargement of the prostate. Market research with physicians, patients, and managed care.
- Assessment of biosimilar opportunity and strategies for response. Market research with payers, hospitals, and physicians.
- Comprehensive review of pricing and contracting strategy across all channels. Market research with payers.
- Development of at-risk contracting strategy.

Wound closure

- Opportunity assessment for novel wound closure technology.
- Contracting strategy for wound closure treatments.
- Opportunity assessment regarding home healthcare and wound closure treatments.

Other

- Global valuation of technology for eye care company.
- Managed care strategy to support the launch of visco-supplementation product. Market research with physicians and managed care.
- Assessment of role for specialty pharmacies in channel management.
- Global assessment of opportunities and infrastructure to support the launch of new vaccine products.
- Assessment and re-design of contracting support operations.
- Product design and bidding strategy for commercial managed care and Medicare Part D provider.
- Opportunity assessment regarding home healthcare and medical gases.

General strategy

- Evolution of managed care and its impact on the pharmaceutical industry.
- Strategy for the retail pharmacy.
- Innovations in managed care contracting.
- Assessment of B2B e-commerce strategy for the pharmaceutical industry.
- Contracting for all manufacturer products with major US PBM.
- Strategy for Medicare Part D.
- Tender pricing strategy and implementation. Pilot test covers Mexico, Brazil, Taiwan, Australia, and UAE.
- Corporate strategy regarding opportunities for cross-company collaboration covering prescription pharmaceuticals, over-the-counter drugs, diagnostics, and vaccines.
- Redesign of business planning capability incorporating local market assessments.
- Redesign of managed markets functions and departments.
- Portfolio positioning strategy for managed care. Market research with managed care.
- Channel stewardship strategy for physician-administered products.
- Opportunity assessment in benefits administration.
- Global portfolio strategy assessment for biosimilars. Market research with payers, pharmacists, and physicians.

Licensing strategy

- Valuation of biologics contract development and manufacturing facility
- Licensing strategy for antibody discovery technology.
- Licensing strategy for orphan drug.

Public policy

- Forced conversion to OTC status.
- Innovation in the pharmaceutical industry: Opportunities for Europe.
- Comparative analysis of access to innovative pharmaceutical products. Countries covered include: US, Australia, Canada, France, Germany, and UK.
- Development of scorecard to assess exposure to pricing pressures.

Honors and awards

Dean’s Doctoral Fellow, Harvard Graduate School of Arts and Sciences/Harvard Graduate School of Business Administration.

George Baker Scholar, John Thayer Scholar, Frank Knox Memorial Fellow, McKenzie King Traveling Scholar, Harvard Graduate School of Business Administration.

Governor General's Gold Medal, Gordon Shrum Scholar, Simon Fraser University.

Exhibit III-1

Ten Most Commonly Prescribed Opioids by MME in the Counties

	Molecule	Common Brand Names for Molecule	Common Combinations and Associated Brands	Formulations	Abuse Deterrent Formulations	DEA Schedule	MME Conversion Factor
	[a]	[b]	[c]	[d]	[e]	[f]	[g]
[1]	Oxycodone	OxyContin	Oxycodone and acetaminophen (Tylox) Oxycodone and aspirin (Percodan) Oxycodone hydrochloride and acetaminophen (Percocet) Oxycodone hydrochloride and ibuprofen	Capsule Solution Tablet	OxyContin Roxybond Targiniq Troxyca ER Xtampza ER	Schedule II	1.50
[2]	Hydrocodone	Hycodan	Hydrocodone bitartrate and homatropine methylbromide Hydrocodone bitartrate and acetaminophen (Lorcet-HD, Lortab, Vicodin) Hydrocodone bitartrate and homatropine methylbromide Hydrocodone bitartrate and ibuprofen (Vicoprofen)	Capsule Solution Suspension Syrup Tablet	Hysingla Vantrela ER	Schedule II	1.00
[3]	Propoxyphene	Darvon	Propoxyphene hydrochloride and acetaminophen Propoxyphene napsylate and acetaminophen (Darvocet-N 100) Propoxyphene hydrochloride w/ aspirin and caffeine	Capsule Suspension Tablet		Schedule IV	0.23
[4]	Fentanyl	Duragesic Sublimaze	Fentanyl citrate and droperidol (Innovar)	Film Injection Patch Lozenge Spray System Tablet		Schedule II	7.20 (Patch) 0.13 (Film; Tablet)
[5]	Tramadol	Ultram	Tramadol hydrochloride and acetaminophen (Ultracet)	Capsule Tablet		Schedule IV	0.10
[6]	Morphine	Kadian MS-Contin MSIR Oramorph SR RMS Roxanol	Morphine sulfate and naltrexone hydrochloride (Embeda)	Capsule Injection Solution Tablet	Arymo ER Embeda Morphabond ER	Schedule II	1.00
[7]	Methadone	Dolophine Methadose		Concentrate Injection Powder Solution Syrup Tablet		Schedule II	3.00
[8]	Codeine		Acetaminophen and codeine phosphate (Tylenol with Codeine) Acetaminophen, aspirin, and codeine phosphate Acetaminophen, caffeine, and dihydrocodeine bitartrate	Capsule Solution Suspension Syrup Tablet		Schedules II, III	0.15
[9]	Oxymorphone	Opana Opana ER		Injection Suppository Tablet		Schedule II	3.00
[10]	Hydromorphone	Dilaudid		Capsule Injection Solution Tablet		Schedule II	4.00

Exhibit III-1 (Continued)

Ten Most Commonly Prescribed Opioids by MME in the Counties

Notes and Sources:

Top opioid molecules in Summit and Cuyahoga counties collectively from IQVIA Xponent Data 1997-2018.
Molecule DEA Schedule based on current DEA classification.

[a] IQVIA Xponent Data.

[b-c] Brand names and combinations are examples provided by the DEA or listed in Orange Book, these are not exhaustive lists.

[e] List of products taken from Adler, Jeremy A. and Theresa Mallick-Searle, "An overview of abuse-deterrent opioids and recommendations for practical patient care," *Journal of Multidisciplinary Healthcare* , 11, 2018, Table 3.

[g] "Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors," CMS, https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Oral-MME-CFs-vFeb-2018.pdf.

[1][b-d] "Oxycodone," DEA, https://www.dea.gov/factsheets/oxycodone; FDA Orange Book, Oxycodone, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm; "Percocet," Endo, http://www.endo.com/File%20Library/Products/Prescribing%20Information/PERCOCET_prescribing_information.html.

[1][e] "FDA Approved Drug Products," Drugs@FDA, NDA 022272, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022272; "FDA Approved Drug Products," Drugs@FDA, NDA 205777, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=205777; "FDA Approved Drug Products," Drugs@FDA, NDA 208090, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=208090; "FDA Approved Drug Products," Drugs@FDA, NDA 209777, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=209777; "FDA Approved Drug Products," Drugs@FDA, NDA 207621, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=207621. I note that Roxybond, Targiniq, and Troxyca ER have since been discontinued.

[1][f] "Practitioner's Manual - SECTION II," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section2.htm.

[2][b-d,f] "Hydrocodone," DEA, https://www.deadiversion.usdoj.gov/drug_chem_info/hydrocodone.pdf; FDA Orange Book, Hydrocodone, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[2][e] "FDA Approved Drug Products," Drugs@FDA, NDA 206627, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=206627; "FDA Approved Drug Products," Drugs@FDA, NDA 207975, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=207975. I note that Vantrela ER has since been discontinued.

[3][b-d,f] "Practitioner's Manual - SECTION II," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section2.htm; FDA Orange Book, Propoxyphene, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[4][b-d,f] "Practitioner's Manual - SECTION II," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section2.htm; FDA Orange Book, Fentanyl, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm; IQVIA Xponent Data.

[5][b-d,f] "Tramadol," DEA, https://www.deadiversion.usdoj.gov/drug_chem_info/tramadol.pdf; FDA Orange Book, Tramadol, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[6][b-d,f] "Morphine," DEA, https://www.dea.gov/factsheets/morphine; FDA Orange Book, Morphine, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[6][e] "FDA Approved Drug Products," Drugs@FDA, NDA 208603, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=208603; "FDA Approved Drug Products," Drugs@FDA, NDA 022321, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022321; "FDA Approved Drug Products," Drugs@FDA, NDA 206544, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=206544. I note that Arymo ER has since been discontinued.

[7][b-d,f] "Methadone," DEA, https://www.deadiversion.usdoj.gov/drug_chem_info/methadone/methadone.pdf; FDA Orange Book, Methadone, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[8][b-d,f] "Practitioner's Manual - SECTION II," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section2.htm; FDA Orange Book, Codeine, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[9][b,f] "Oxymorphone," DEA, https://www.deadiversion.usdoj.gov/drug_chem_info/oxymorphone.pdf; FDA Orange Book, Oxymorphone, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[10][b-d] "Hydromorphone," DEA, https://www.dea.gov/factsheets/hydromorphone; FDA Orange Book, Hydromorphone, https://www.accessdata.fda.gov/Scripts/cder/ob/search_product.cfm.

[10][f] "Practitioner's Manual - SECTION II," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section2.htm.

Exhibit III-2

Ten Most Commonly Prescribed Opioids by MME, Nationally
2001, 2006, 2011, 2016

2001

Rank	Product Group	MME	% of Total
1	Propoxyphene	30,229,431,401	27.1%
2	Oxycodone	27,948,888,315	25.1%
3	Hydrocodone	22,344,362,100	20.0%
4	Fentanyl	9,255,237,757	8.3%
5	Morphine	6,651,741,946	6.0%
6	Methadone	5,132,925,599	4.6%
7	Tramadol	4,179,591,997	3.7%
8	Codeine	4,142,826,062	3.7%
9	Pentazocine	594,577,824	0.5%
10	Hydromorphone	528,054,406	0.5%
	All Opioids	111,534,169,248	100.0%

2006

Rank	Product Group	MME	% of Total
1	Oxycodone	51,273,134,098	27.5%
2	Hydrocodone	39,256,223,388	21.1%
3	Propoxyphene	26,903,217,489	14.4%
4	Fentanyl	24,123,376,700	12.9%
5	Methadone	16,421,749,325	8.8%
6	Morphine	14,639,110,992	7.9%
7	Tramadol	7,607,555,681	4.1%
8	Codeine	3,222,023,804	1.7%
9	Hydromorphone	1,982,410,995	1.1%
10	Pentazocine	400,498,878	0.2%
	All Opioids	186,345,635,562	100.0%

2011

Rank	Product Group	MME	% of Total
1	Oxycodone	92,140,111,477	37.9%
2	Hydrocodone	56,628,057,330	23.3%
3	Fentanyl	24,454,301,690	10.1%
4	Morphine	22,601,748,801	9.3%
5	Methadone	17,639,029,147	7.2%
6	Tramadol	13,192,285,137	5.4%
7	Oxymorphone	6,980,750,306	2.9%
8	Hydromorphone	4,407,484,029	1.8%
9	Codeine	2,802,646,282	1.2%
10	Tapentadol	1,893,302,821	0.8%
	All Opioids	243,306,711,194	100.0%

2016

Rank	Product Group	MME	% of Total
1	Oxycodone	75,910,161,466	38.8%
2	Hydrocodone	42,370,904,729	21.7%
3	Fentanyl	19,497,329,623	10.0%
4	Morphine	18,595,372,738	9.5%
5	Tramadol	15,345,556,949	7.8%
6	Methadone	9,328,157,164	4.8%
7	Oxymorphone	4,489,950,050	2.3%
8	Hydromorphone	4,407,401,107	2.3%
9	Codeine	3,084,036,133	1.6%
10	Tapentadol	2,226,226,469	1.1%
	All Opioids	195,549,111,541	100.0%

Notes and Sources:

IQVIA Xponent Data.

Exhibit III-3

Ten Most Commonly Prescribed Opioids by MME, Cuyahoga County
2001, 2006, 2011, 2016

2001

Rank	Product Group	MME	% of Total
1	Propoxyphene	192,747,462	35.9%
2	Oxycodone	145,711,185	27.2%
3	Hydrocodone	68,030,952	12.7%
4	Fentanyl	39,592,958	7.4%
5	Morphine	26,575,797	5.0%
6	Tramadol	25,629,109	4.8%
7	Codeine	22,691,261	4.2%
8	Methadone	7,817,721	1.5%
9	Pentazocine	3,416,460	0.6%
10	Hydromorphone	1,605,836	0.3%
	All Opioids	536,453,834	100.0%

2006

Rank	Product Group	MME	% of Total
1	Oxycodone	291,198,085	32.4%
2	Propoxyphene	174,855,881	19.5%
3	Hydrocodone	120,464,632	13.4%
4	Fentanyl	99,390,472	11.1%
5	Methadone	67,149,512	7.5%
6	Morphine	59,280,442	6.6%
7	Tramadol	53,832,563	6.0%
8	Codeine	19,109,770	2.1%
9	Hydromorphone	7,873,431	0.9%
10	Pentazocine	1,835,554	0.2%
	All Opioids	897,481,894	100.0%

2011

Rank	Product Group	MME	% of Total
1	Oxycodone	433,937,187	40.7%
2	Hydrocodone	183,001,408	17.2%
3	Fentanyl	103,973,134	9.8%
4	Tramadol	88,147,206	8.3%
5	Morphine	81,078,819	7.6%
6	Methadone	67,302,094	6.3%
7	Oxymorphone	57,355,547	5.4%
8	Hydromorphone	17,718,343	1.7%
9	Codeine	16,381,680	1.5%
10	Tapentadol	14,732,689	1.4%
	All Opioids	1,065,186,527	100.0%

2016

Rank	Product Group	MME	% of Total
1	Oxycodone	331,614,334	43.7%
2	Hydrocodone	124,565,682	16.4%
3	Tramadol	88,226,147	11.6%
4	Fentanyl	64,863,794	8.5%
5	Morphine	60,338,533	7.9%
6	Methadone	38,572,707	5.1%
7	Hydromorphone	14,057,747	1.9%
8	Oxymorphone	12,869,677	1.7%
9	Tapentadol	11,789,801	1.6%
10	Codeine	11,452,833	1.5%
	All Opioids	759,032,252	100.0%

Notes and Sources:

IQVIA Xponent Data.

Exhibit III-4

Ten Most Commonly Prescribed Opioids by MME, Summit County
2001, 2006, 2011, 2016

2001

Rank	Product Group	MME	% of Total
1	Propoxyphene	113,868,688	33.9%
2	Oxycodone	90,808,438	27.0%
3	Hydrocodone	46,381,422	13.8%
4	Fentanyl	37,887,118	11.3%
5	Morphine	16,910,228	5.0%
6	Tramadol	14,412,964	4.3%
7	Codeine	8,406,195	2.5%
8	Methadone	3,192,261	0.9%
9	Pentazocine	2,604,258	0.8%
10	Hydromorphone	989,034	0.3%
	All Opioids	336,391,786	100.0%

2006

Rank	Product Group	MME	% of Total
1	Oxycodone	148,993,235	32.9%
2	Propoxyphene	100,226,926	22.1%
3	Hydrocodone	76,422,862	16.9%
4	Fentanyl	47,077,021	10.4%
5	Morphine	28,922,409	6.4%
6	Tramadol	24,451,721	5.4%
7	Methadone	12,337,112	2.7%
8	Codeine	6,606,281	1.5%
9	Hydromorphone	5,328,980	1.2%
10	Pentazocine	1,618,759	0.4%
	All Opioids	452,768,898	100.0%

2011

Rank	Product Group	MME	% of Total
1	Oxycodone	282,717,972	41.9%
2	Hydrocodone	113,913,870	16.9%
3	Morphine	79,819,314	11.8%
4	Fentanyl	63,842,970	9.5%
5	Tramadol	42,095,124	6.2%
6	Oxymorphone	38,692,534	5.7%
7	Methadone	29,573,436	4.4%
8	Hydromorphone	14,774,512	2.2%
9	Codeine	5,932,834	0.9%
10	Tapentadol	1,965,069	0.3%
	All Opioids	674,311,841	100.0%

2016

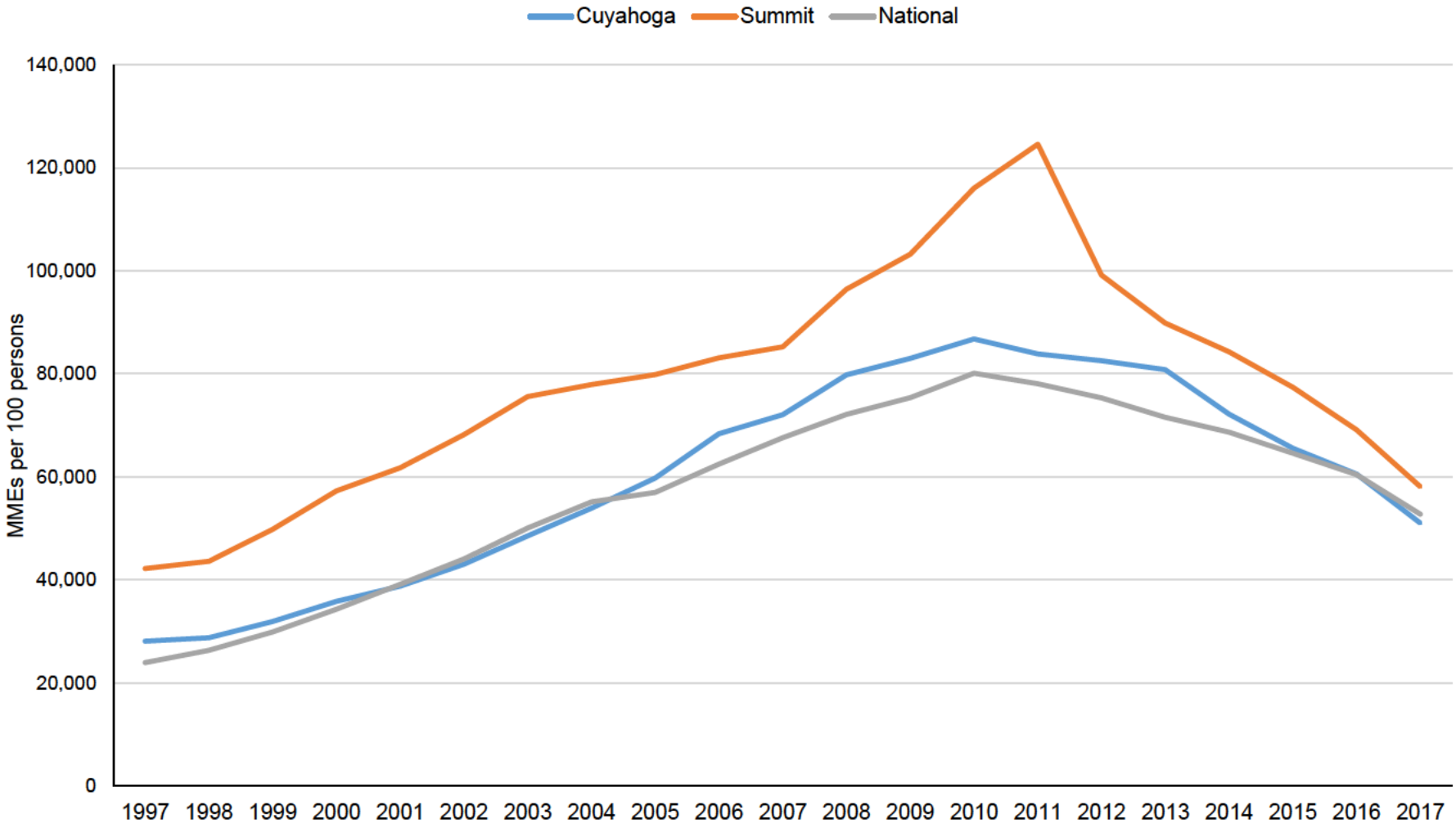
Rank	Product Group	MME	% of Total
1	Oxycodone	173,856,605	46.5%
2	Hydrocodone	71,762,791	19.2%
3	Tramadol	37,477,076	10.0%
4	Morphine	31,456,996	8.4%
5	Fentanyl	24,159,489	6.5%
6	Methadone	12,211,943	3.3%
7	Hydromorphone	8,507,974	2.3%
8	Oxymorphone	5,900,495	1.6%
9	Tapentadol	4,240,800	1.1%
10	Codeine	3,714,491	1.0%
	All Opioids	373,540,307	100.0%

Notes and Sources:

IQVIA Xponent Data.

Exhibit III-5

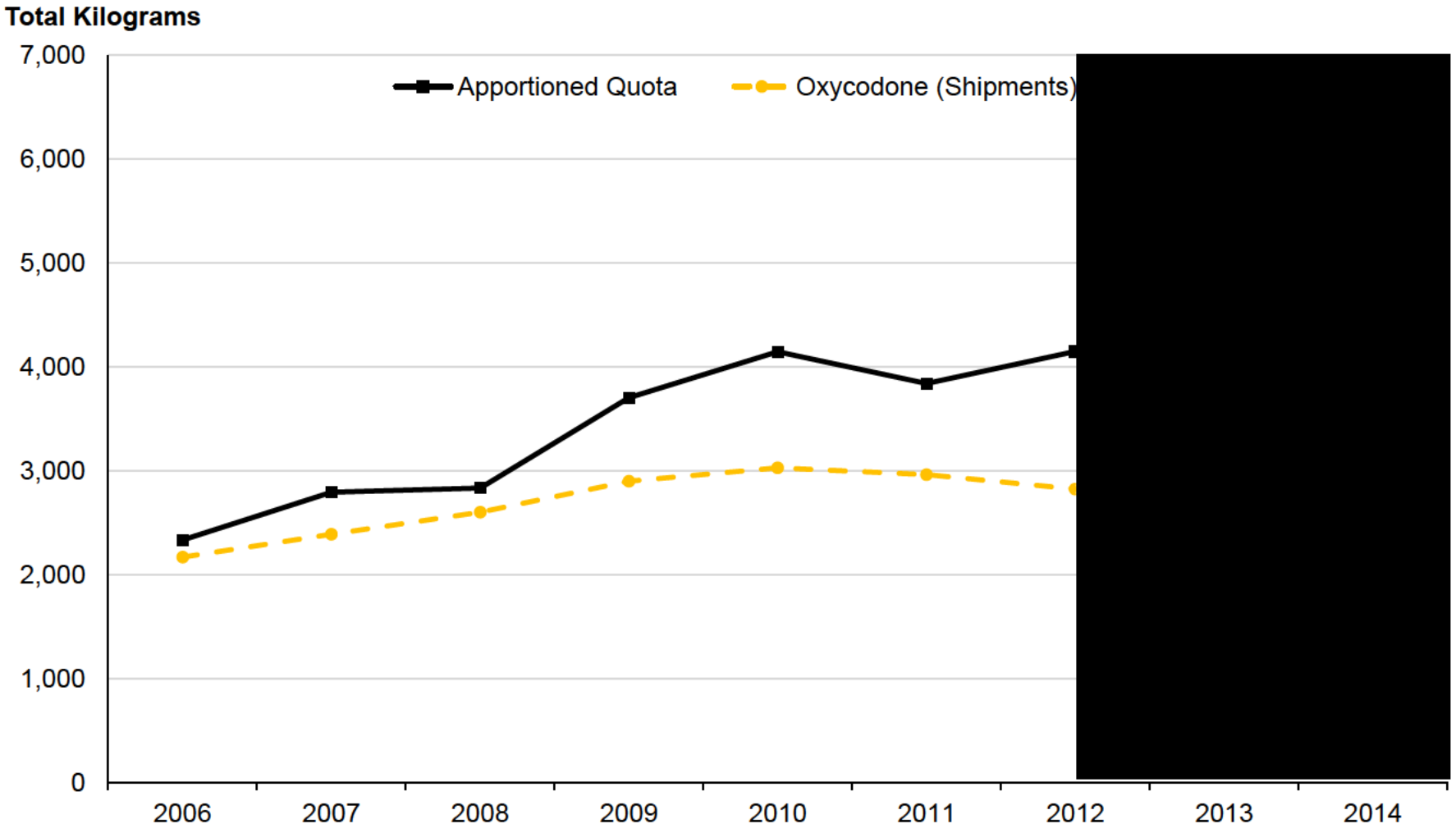
Opioid MME Prescribing Rate per 100 Persons, 1997-2017



Notes and Sources:
IQVIA Xponent Data (for prescribing); SEER Data (for population).
Each line represents total MME prescribing in that geography divided by total population in that geography.

Exhibit III-6

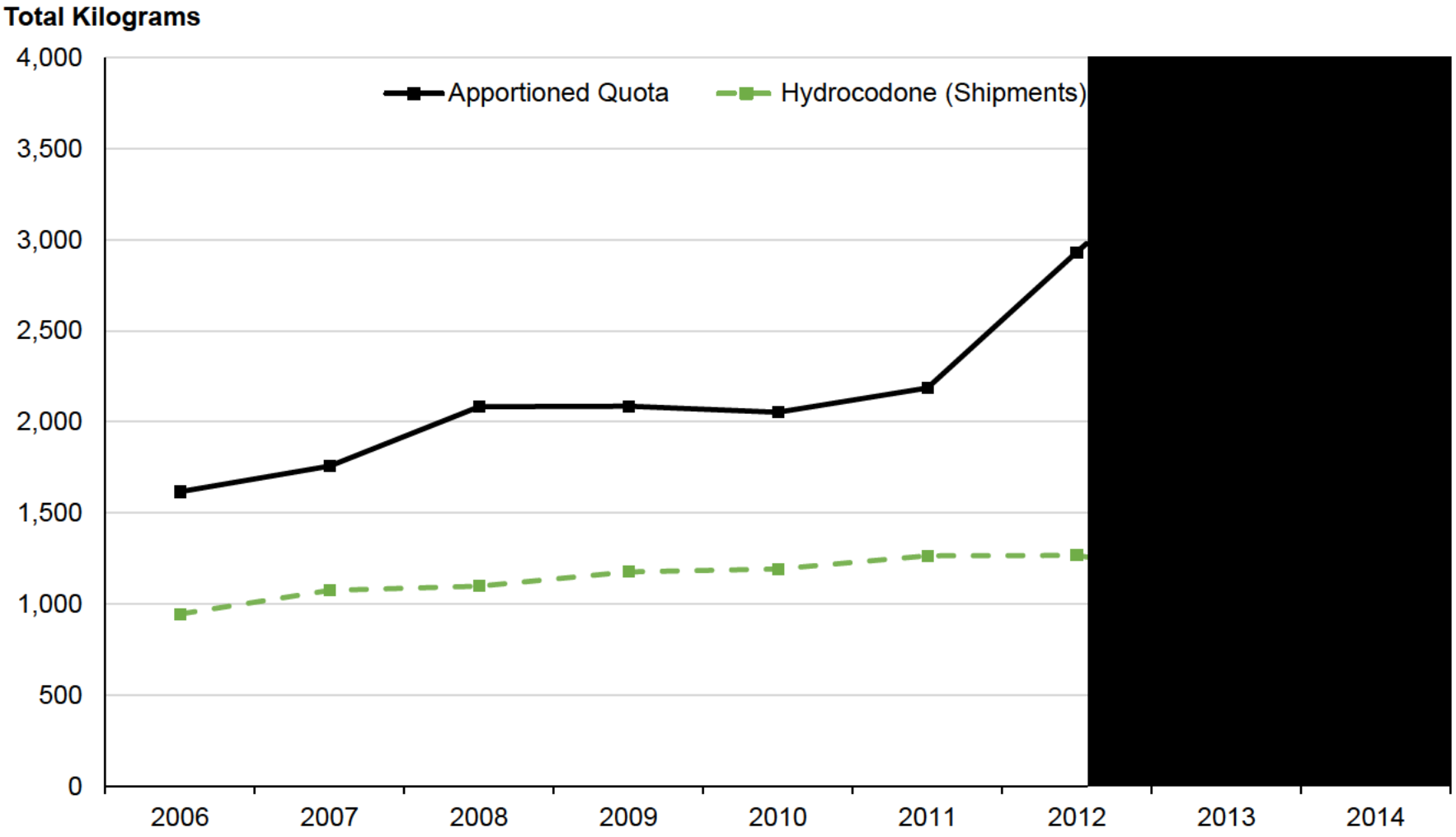
DEA Quotas and Total Shipments to Patient-Facing Customers
Oxycodone; Ohio; 2006-2014



Notes and Sources:
ARCOS Data (for opioid shipments); DEA Quota Data (for drug quotas); SEER Data (for population).
Apportioned Quota is the national quota apportioned by Ohio's share of US population in each year.

Exhibit III-7

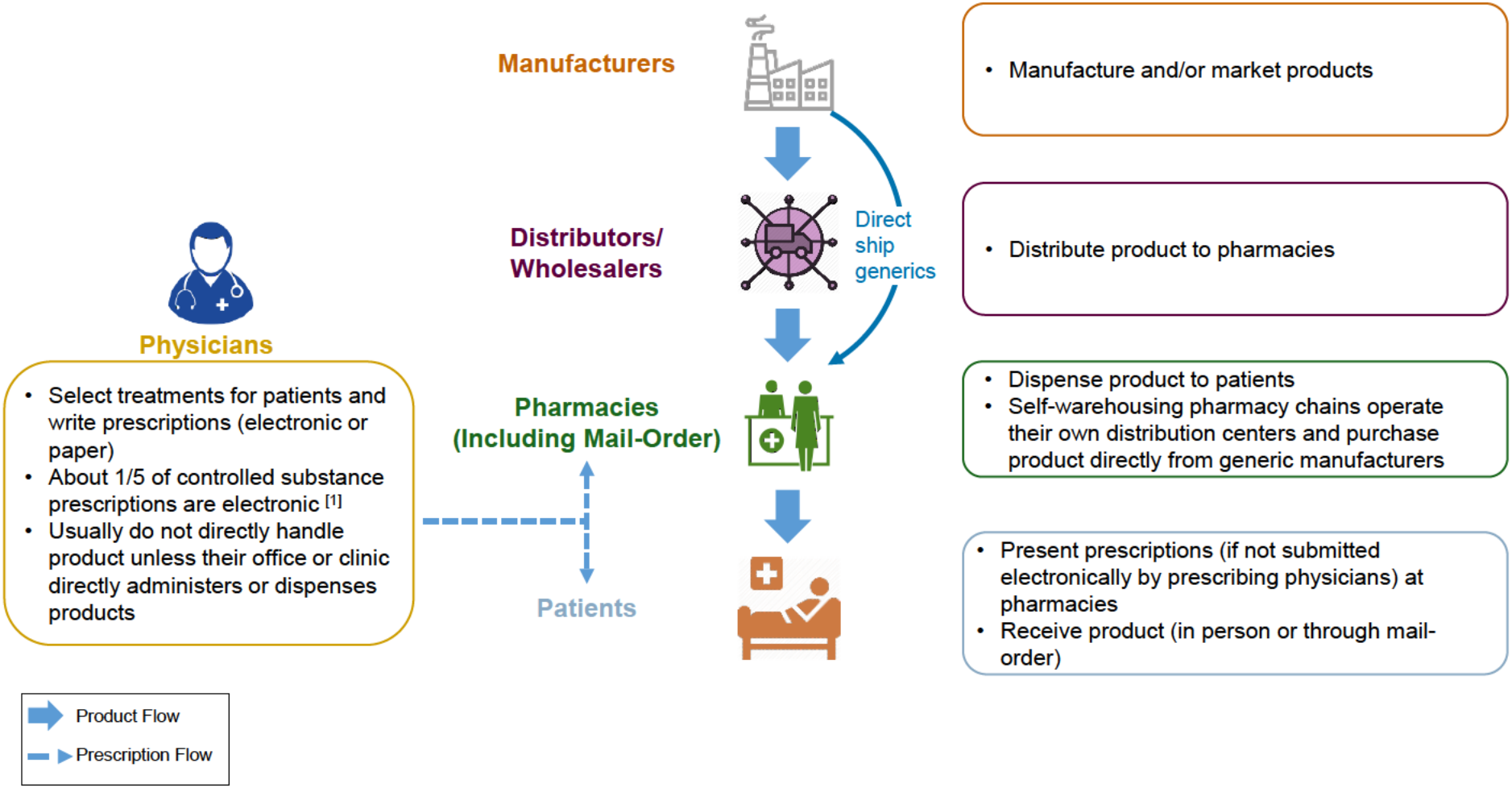
DEA Quotas and Total Shipments to Patient-Facing Customers
Hydrocodone; Ohio; 2006-2014



Notes and Sources:
ARCOS Data (for opioid shipments); DEA Quota Data (for drug quotas); SEER Data (for population).
Apportioned Quota is the national quota apportioned by Ohio's share of US population in each year.

Exhibit IV-1:

Flow of Products



Notes and Sources:

Unless otherwise stated, Bell Report, Section IV.

[1] "2017 National Progress Report," Surescripts, https://surescripts.com/docs/default-source/national-progress-reports/2151_npr_2017_finalB.pdf, p. 6.

Exhibit IV-2:

Flow of Payment

Manufacturers

- Set a wholesale price for the product
- Collect net price due to discounts and rebates

Distributors/ Wholesalers

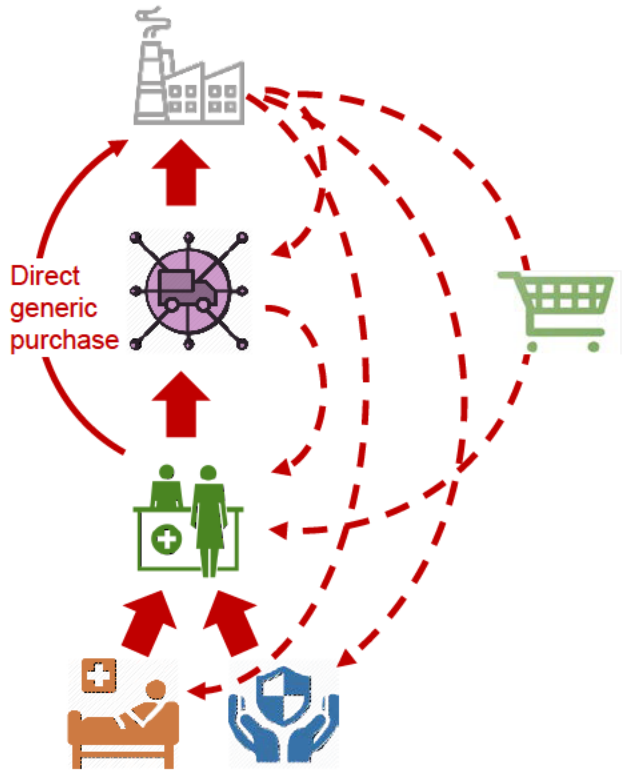
- Pay manufacturers for product
- Provide and charge back manufacturer discounts to pharmacies
- Purchases product at WAC, typically less a prompt pay discount.

Pharmacies (Including Mail-Order)

- Pay wholesalers and/or generic manufacturers for product (may have a special contract price for generics)
- Receive discounts from generic manufacturers (including via wholesalers)

Patients

- Pay cost-sharing (or full price) to pharmacy
- May receive manufacturer assistance towards payment (e.g. copay cards for branded products only)



Some stakeholders influence price through **negotiation**, even if they are not directly involved in payments

Pharmacy Buying Groups and Group Purchasing Organizations

- Negotiate prices with **manufacturers** on behalf of **retail pharmacies and institutions**, respectively

Insurers, Health Plans, Government Payors, and PBMs

- Pay pharmacy pre-negotiated price for covered patients
- May have an in-house mail-order pharmacy
- Negotiate rebates and formulary design with **manufacturers**

Payment Flow

Possible Payment Flow

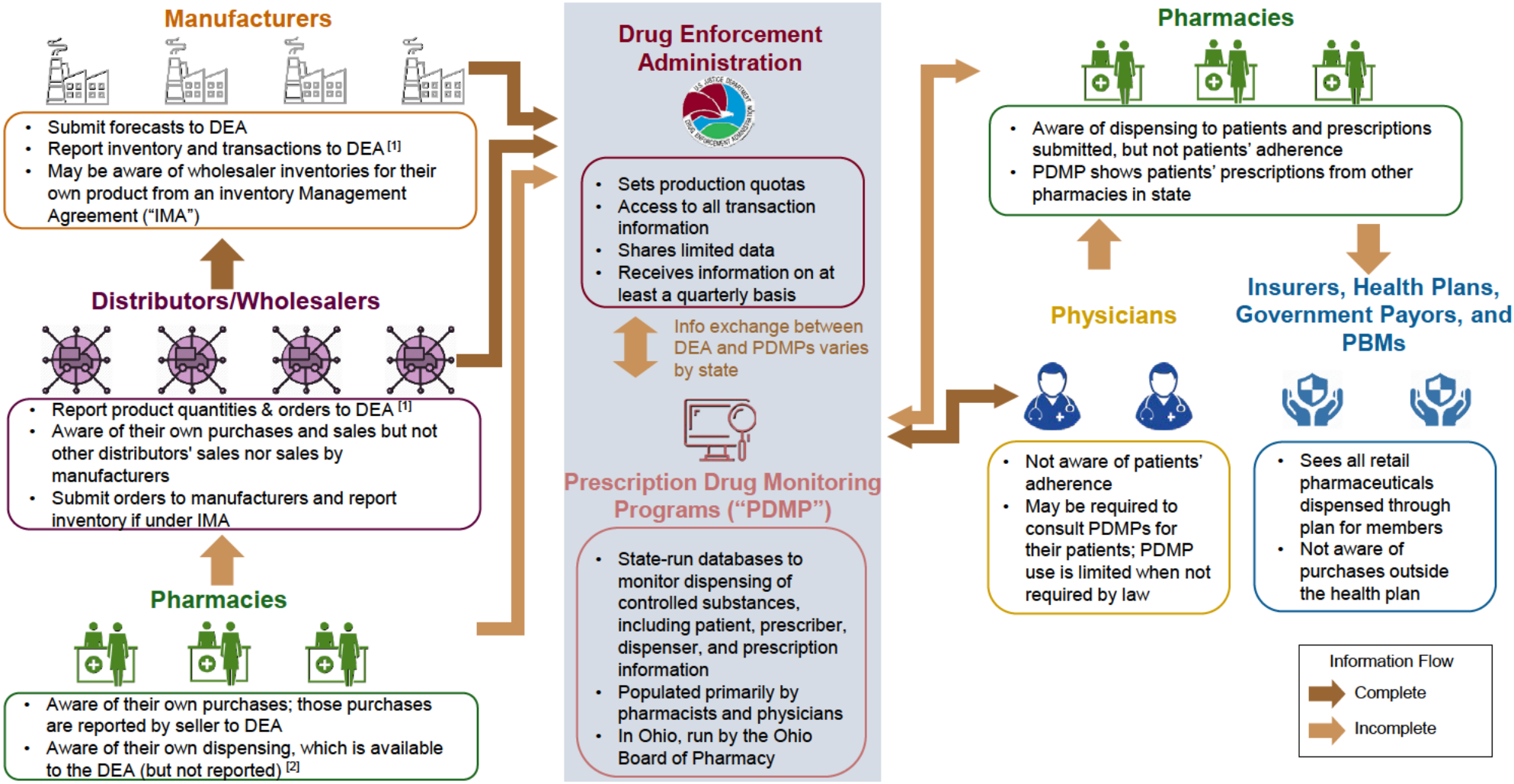
Physicians

- Reimbursed by health plans & patient cost sharing for visit costs, but do not provide or receive any product or prescription-associated payments

Notes and Sources:

Unless otherwise stated, Bell Report, Section IV.

Exhibit IV-3:
Flow of Information



Notes and Sources:

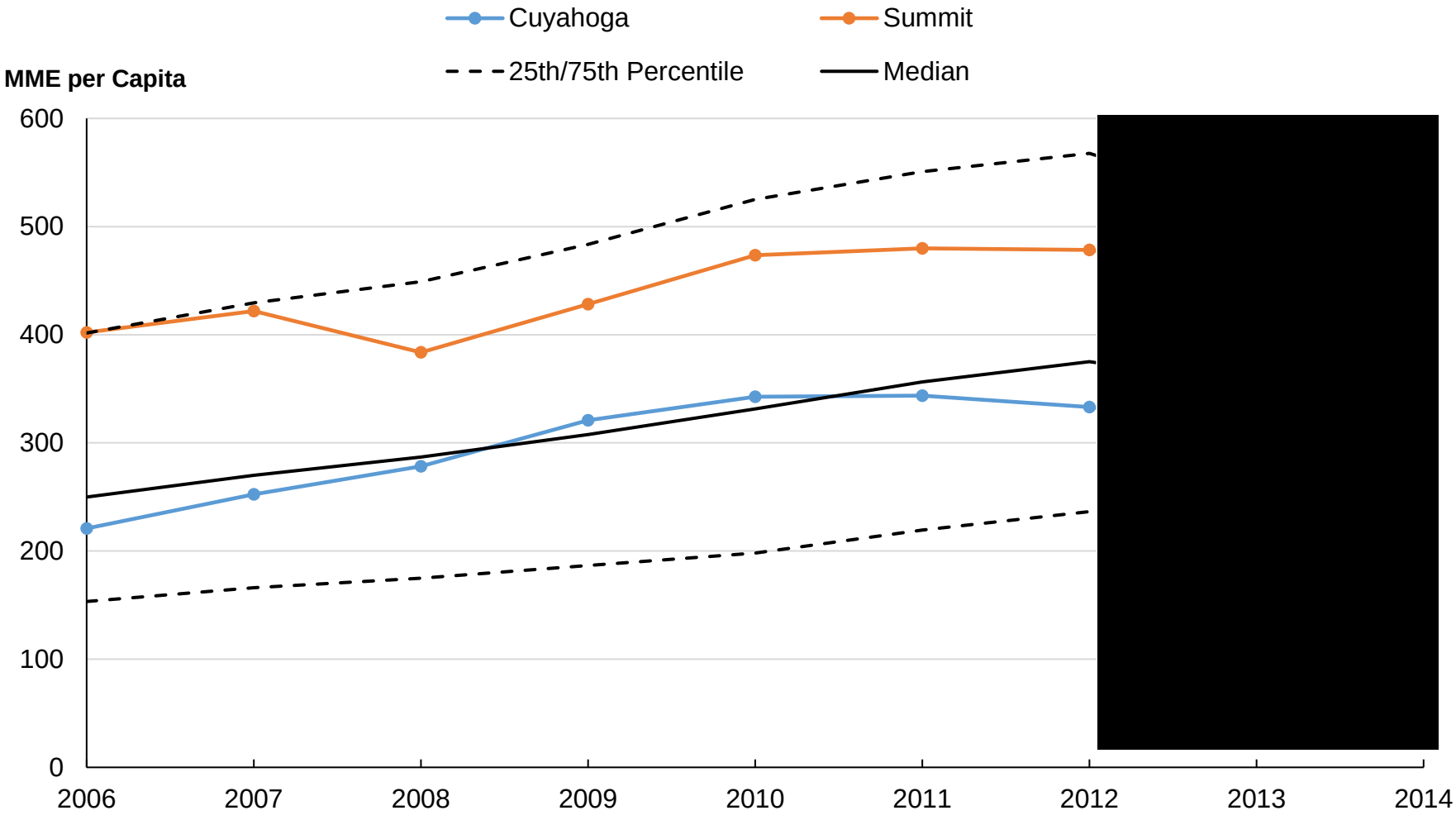
Unless otherwise stated, Bell Report, Section IV.

[1] "ARCOS Registrant Handbook," DEA, https://www.deadiversion.usdoj.gov/arcos/handbook/full.pdf.

[2] "Pharmacist's Manual - Section IX - XIV," DEA, https://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/pharm_content.htm.

Exhibit VI-1

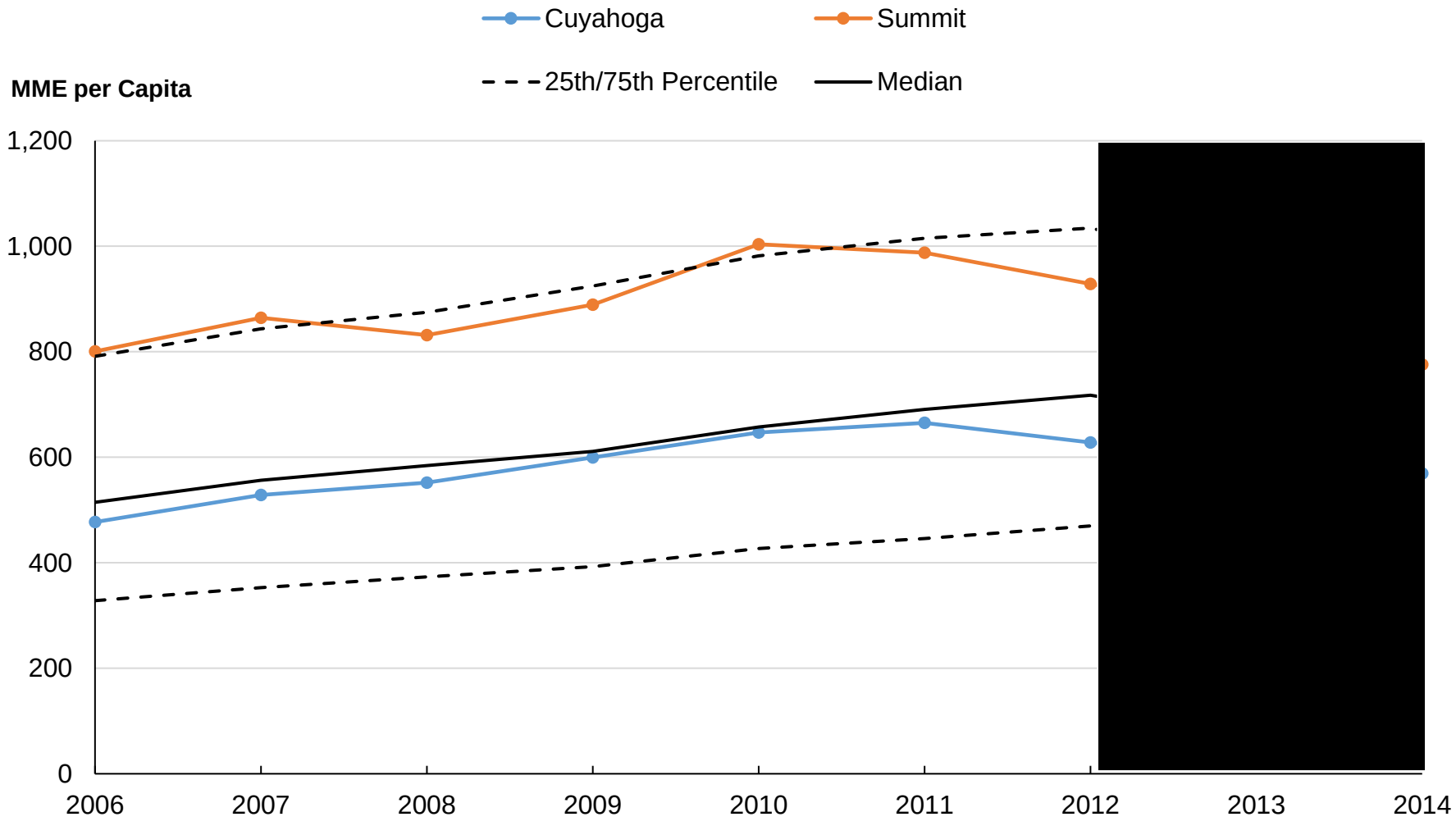
MME Shipments per Capita to the Counties
Oxycodone and Hydrocodone, 2006-2014



Notes and Sources:
ARCOS Data (for opioid shipments); SEER Data (for population).

Exhibit VI-2

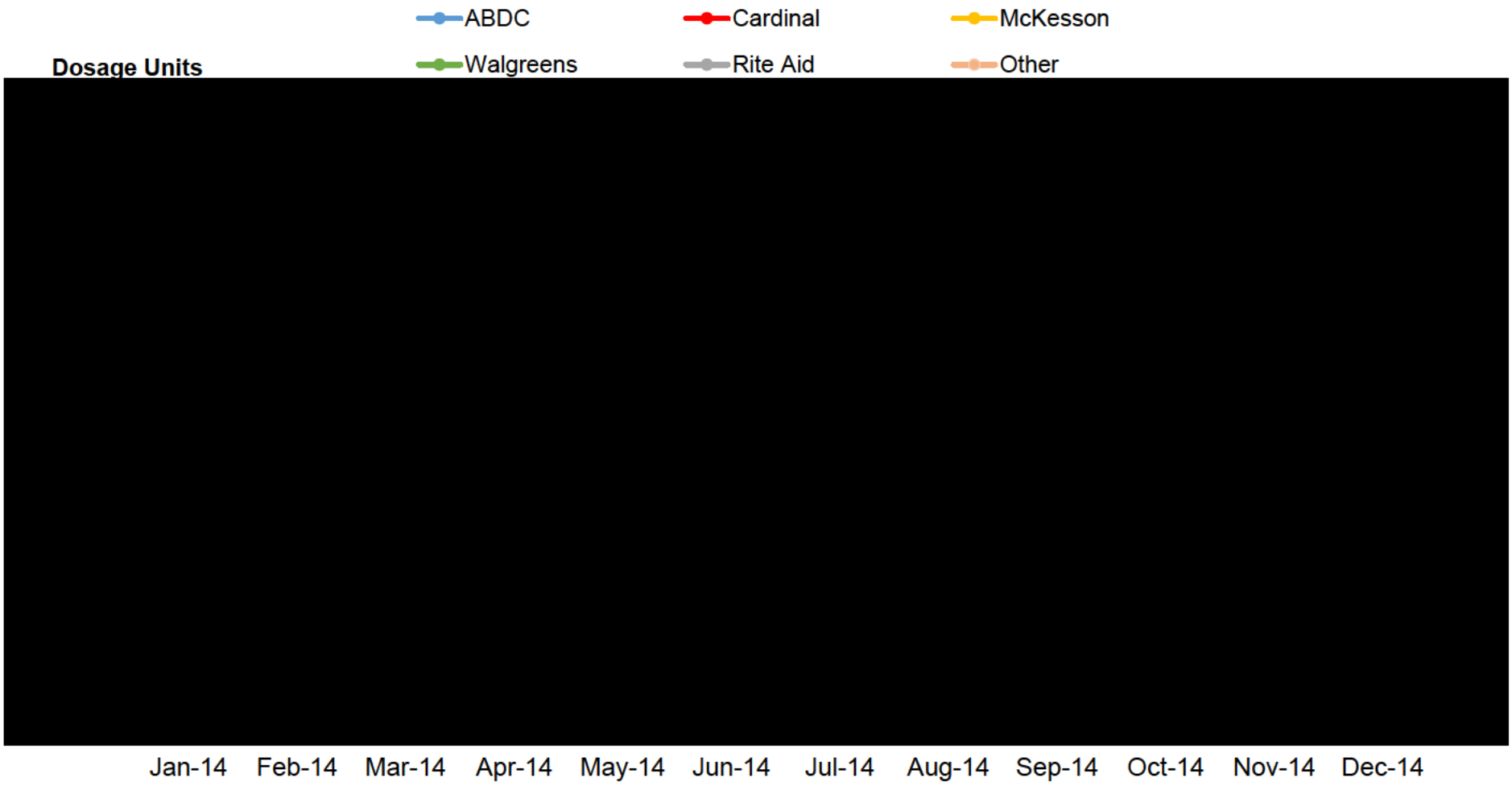
MME Shipments per Capita to the Counties
All Opioids, 2006-2014



Notes and Sources:
ARCOS Data (for opioid shipments); SEER Data (for population)
Sample excludes shipments of buprenorphine.

Exhibit VI-3

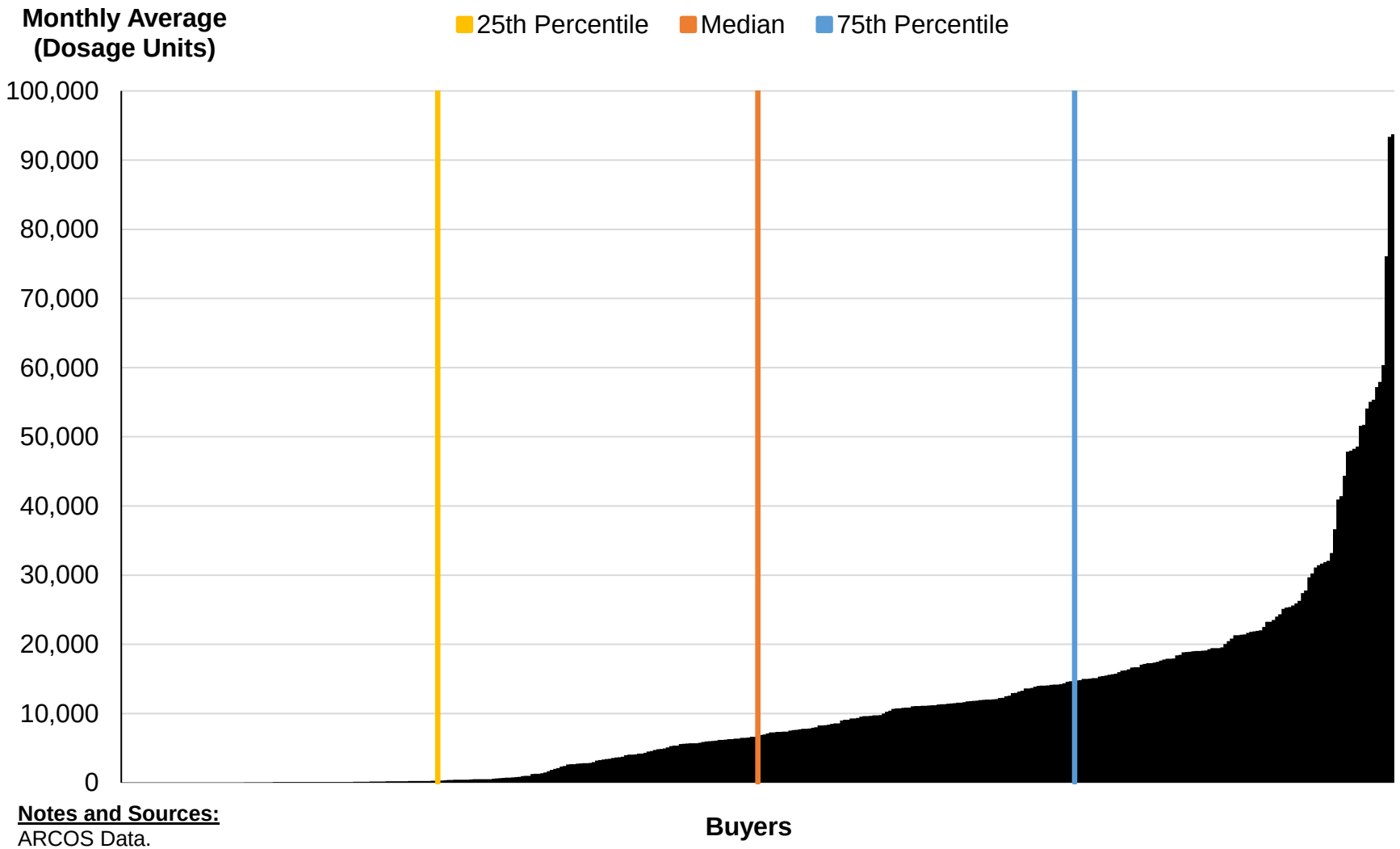
Hydrocodone Shipments by Distributor
Cuyahoga and Summit Counties, 2014



Notes and Sources:
ARCOS Data; "Proposed Rule: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II,", DEA, https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0227.htm; " Final Rule: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II," DEA, https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm.

Exhibit VI-4

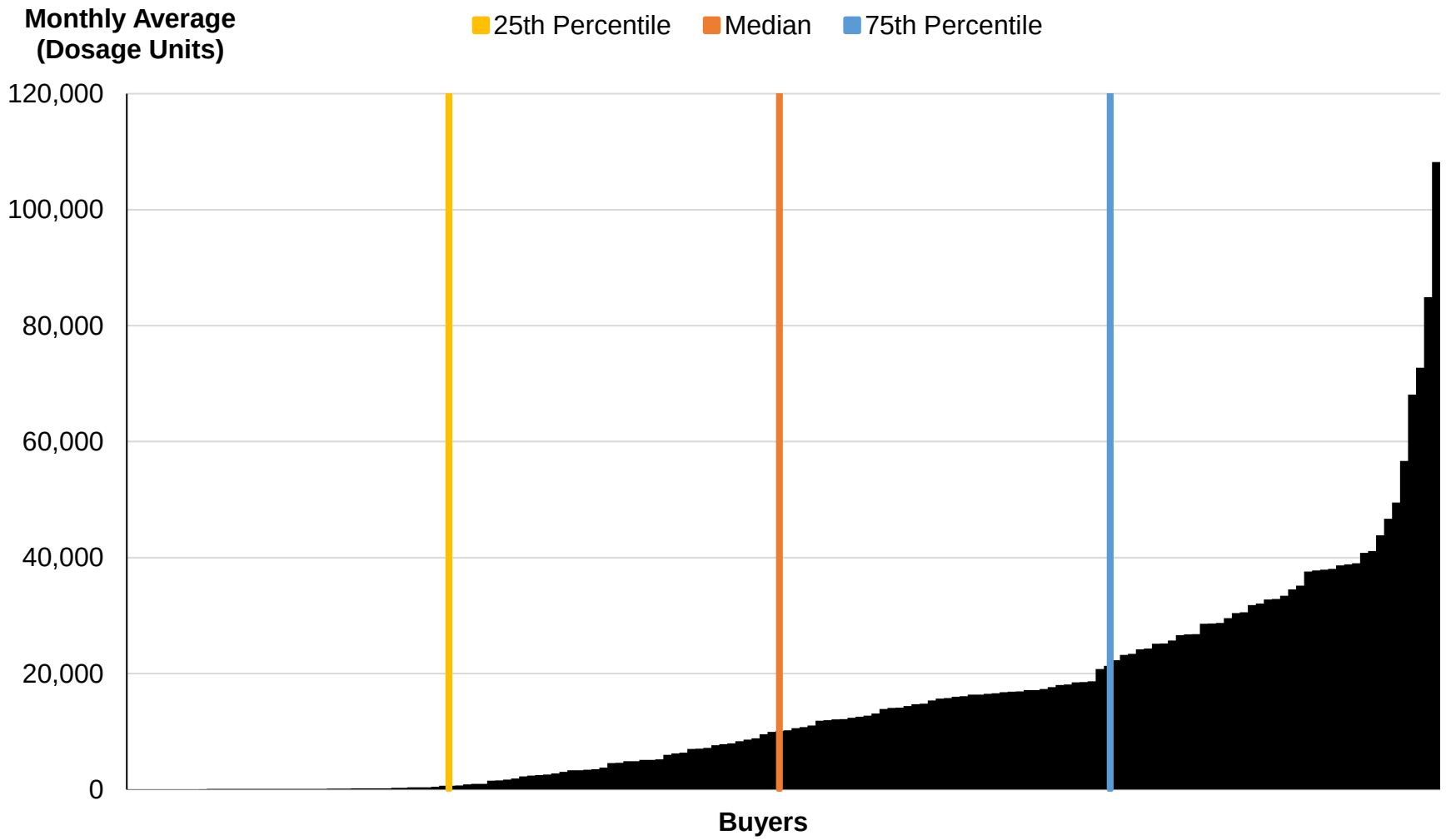
Average Monthly Shipments of Oxycodone and Hydrocodone
Cuyahoga County, 2012



Notes and Sources:
ARCOS Data.
"Monthly Average" is equal to the average total dosage units for a given buyer across all months in 2012 with positive orders. The sample is limited to buyers in Cuyahoga County. Each observation along the x-axis corresponds to a different buyer.

Exhibit VI-5

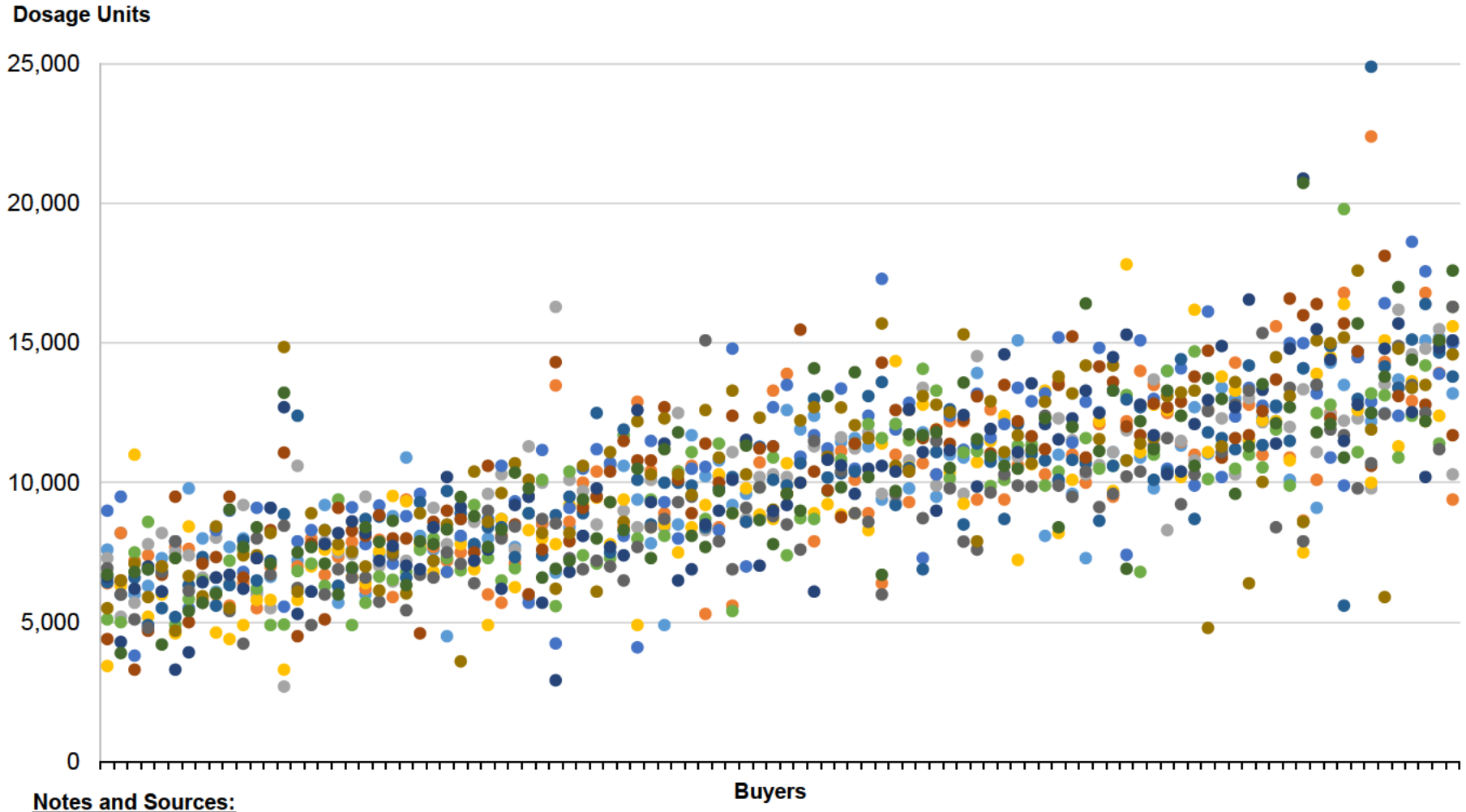
Average Monthly Shipments of Oxycodone and Hydrocodone
Summit County, 2012



Notes and Sources:
ARCOS Data.
"Monthly Average" is equal to the average total dosage units for a given buyer across all months in 2012 with positive orders. The sample is limited to buyers in Summit County. Each observation along the x-axis corresponds to a different buyer.

Exhibit VI-6

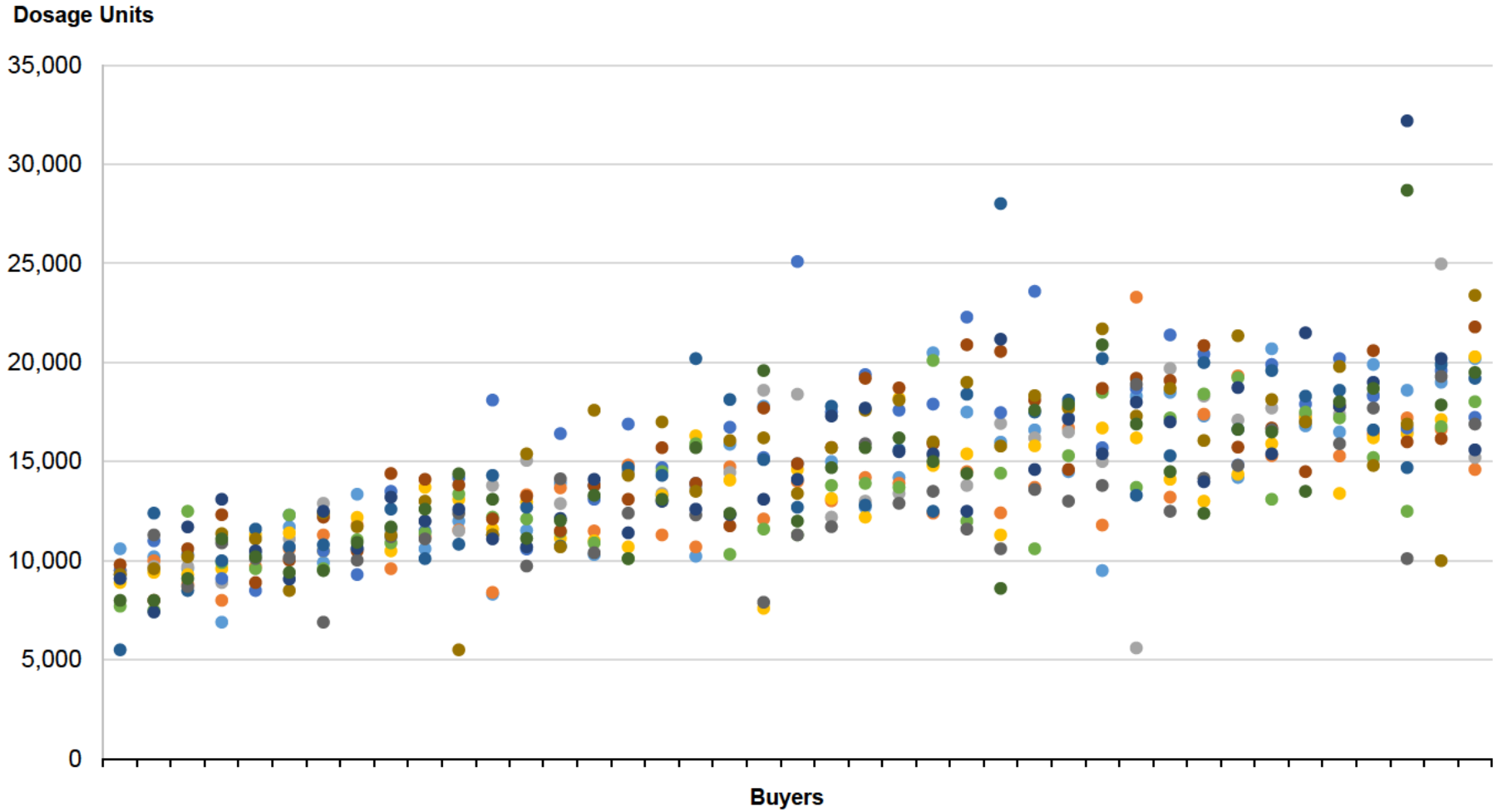
Monthly Orders of Oxycodone and Hydrocodone
Cuyahoga County, 2012



Notes and Sources:
ARCOS Data.
Each dot corresponds to total dosage units ordered by that pharmacy in a given month. Sample is limited to pharmacies in Cuyahoga County for which total prescribing in 2012 falls between the 50th and 75th percentiles of annual dosage units ordered across all pharmacies in the county. Each observation along the x-axis corresponds to a different buyer.

Exhibit VI-7

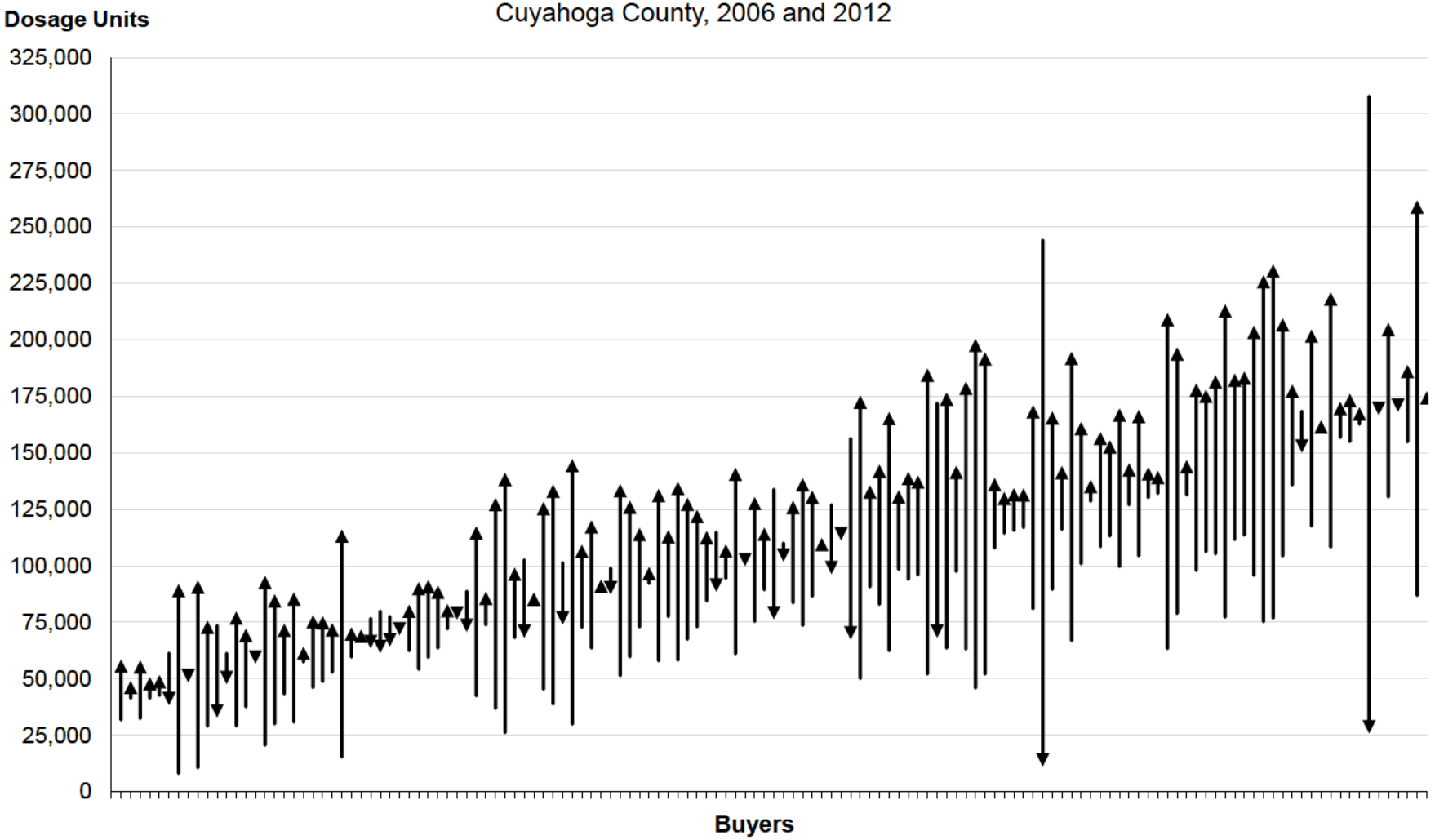
Monthly Orders of Oxycodone and Hydrocodone
Summit County, 2012



Notes and Sources:
ARCOS Data.
Each dot corresponds to total dosage units ordered by that pharmacy in a given month. Sample is limited to pharmacies in Summit County for which total prescribing in 2012 falls between the 50th and 75th percentiles of annual dosage units across all pharmacies in the county. Each observation along the x-axis corresponds to a different buyer.

Exhibit VI-8

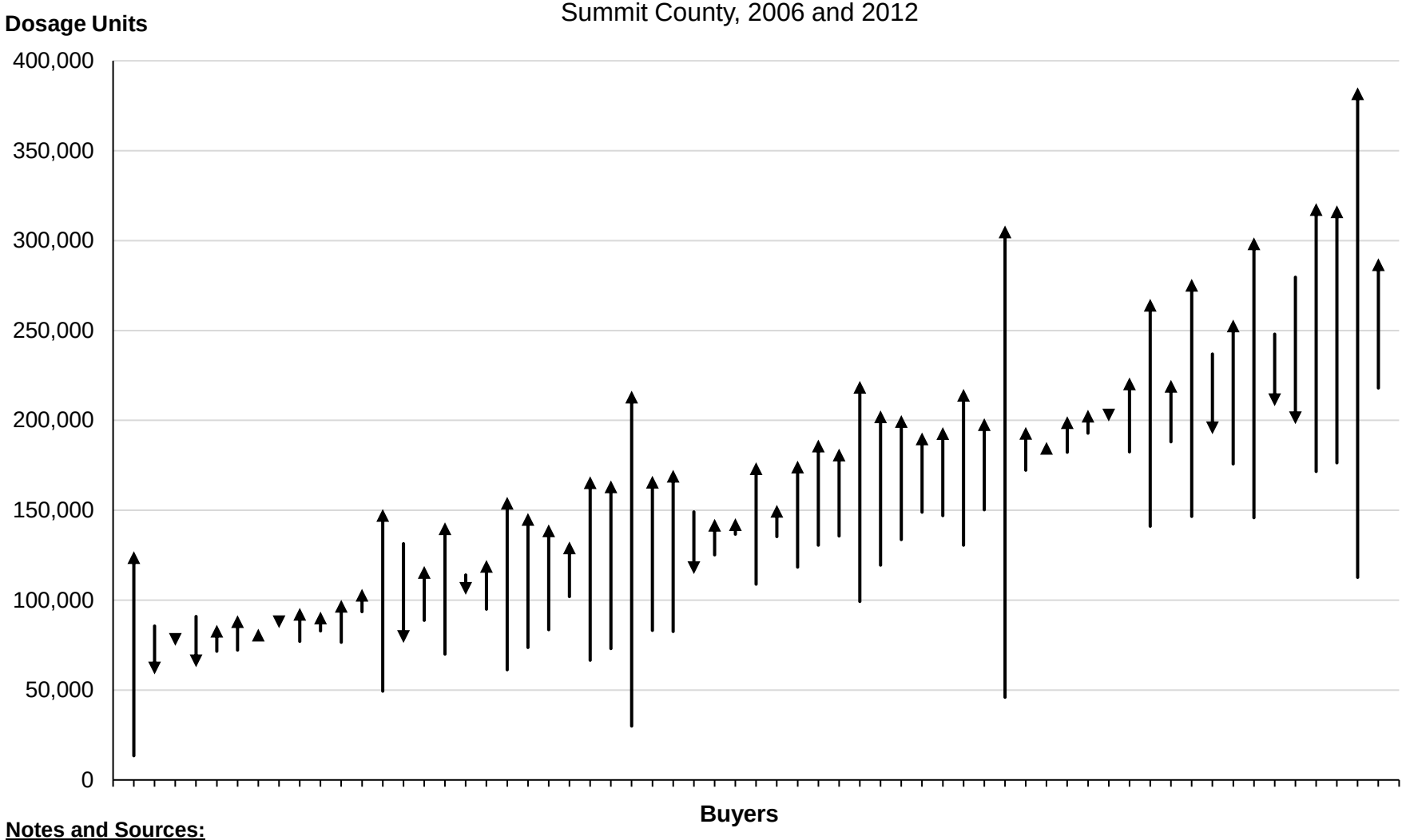
Change in Orders of Oxycodone and Hydrocodone
Cuyahoga County, 2006 and 2012



Notes and Sources:
ARCOS Data.
Each arrow corresponds to the total dosage units ordered by a given buyer in 2006 and 2012. The direction of the arrow indicates the change in orders between 2006 (beginning of the arrow) and 2012 (end of the arrow). Sample is limited to buyers in Cuyahoga County whose combined total prescribing in 2006 and 2012 falls between the 25th and 75th percentiles.

Exhibit VI-9

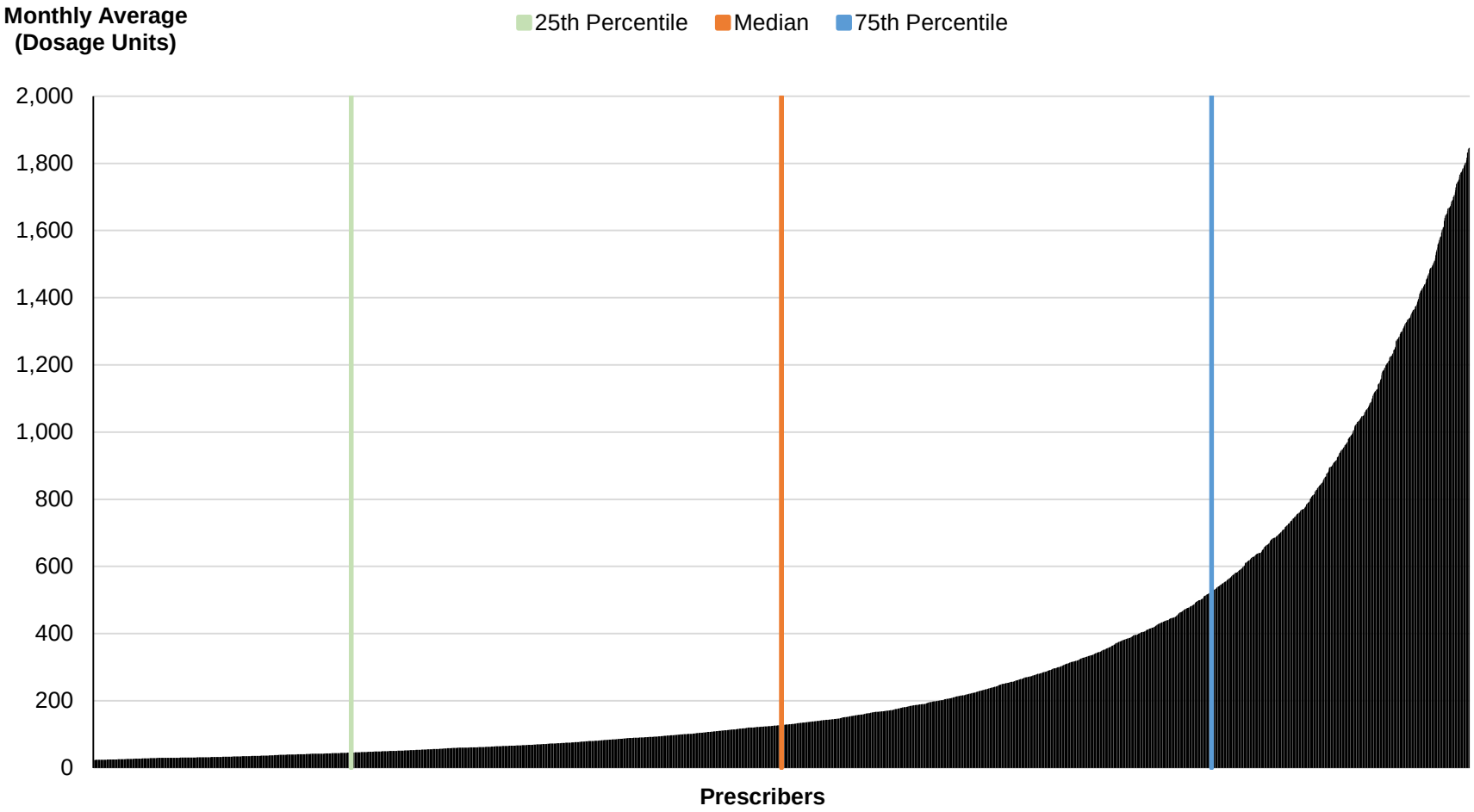
Change in Orders of Oxycodone and Hydrocodone by Pharmacy
Summit County, 2006 and 2012



Notes and Sources:
ARCOS Data.
Each arrow corresponds to the total dosage units ordered by a given buyer in 2006 and 2012. The direction of the arrow indicates the change in orders between 2006 (beginning of the arrow) and 2012 (end of the arrow). Sample is limited to buyers in Summit County whose combined total prescribing in 2006 and 2012 falls between the 25th and 75th percentiles.

Exhibit VI-10

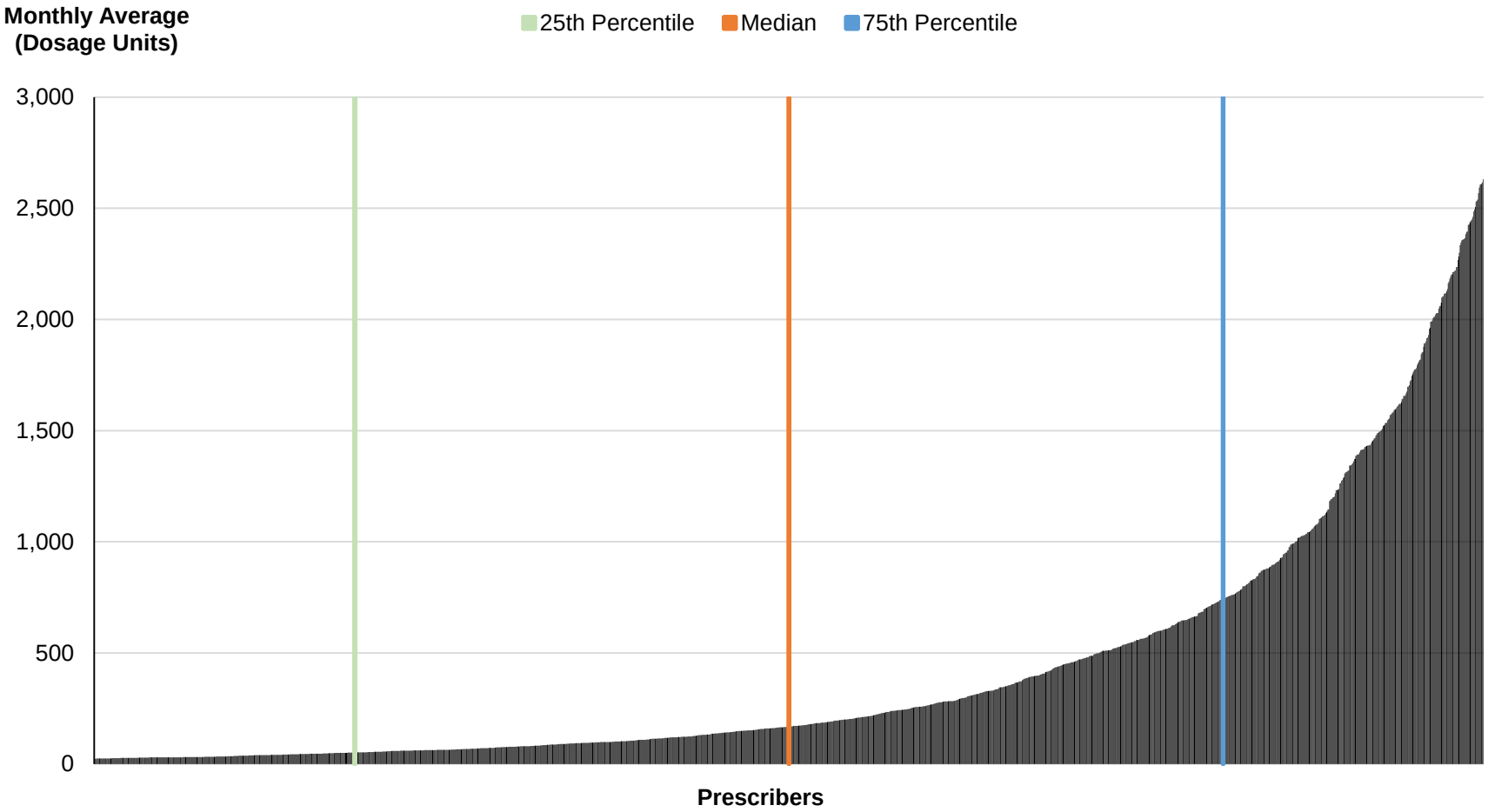
Average Monthly Oxycodone and Hydrocodone Dosage Units Prescribed
Cuyahoga County, 2012



Notes and Sources:
IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622.
"Monthly Average" is equal to the average total dosage units for a given prescriber across all months in 2012 with positive prescribing. The sample is limited to prescribers in Cuyahoga County from the 10th to 90th percentiles. Each observation along the x-axis corresponds to a different prescriber.

Exhibit VI-11

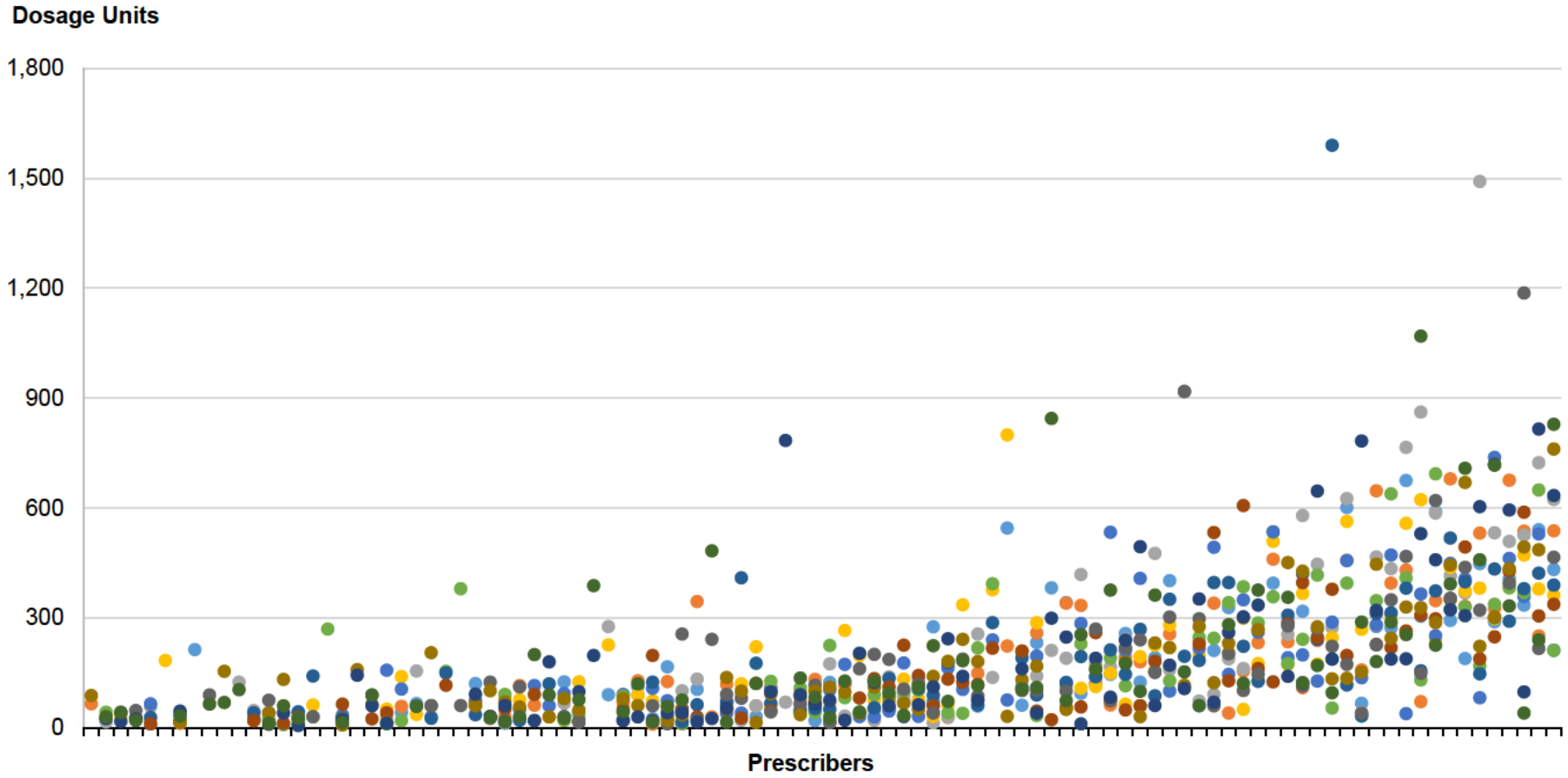
Average Monthly Oxycodone and Hydrocodone Dosage Units Prescribed
Summit County, 2012



Notes and Sources:
IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622.
"Monthly Average" is equal to the average total dosage units for a given prescriber across all months in 2012 with positive prescribing. The sample is limited to prescribers in Summit County from the 10th to 90th percentiles. Each observation along the x-axis corresponds to a different prescriber.

Exhibit VI-12

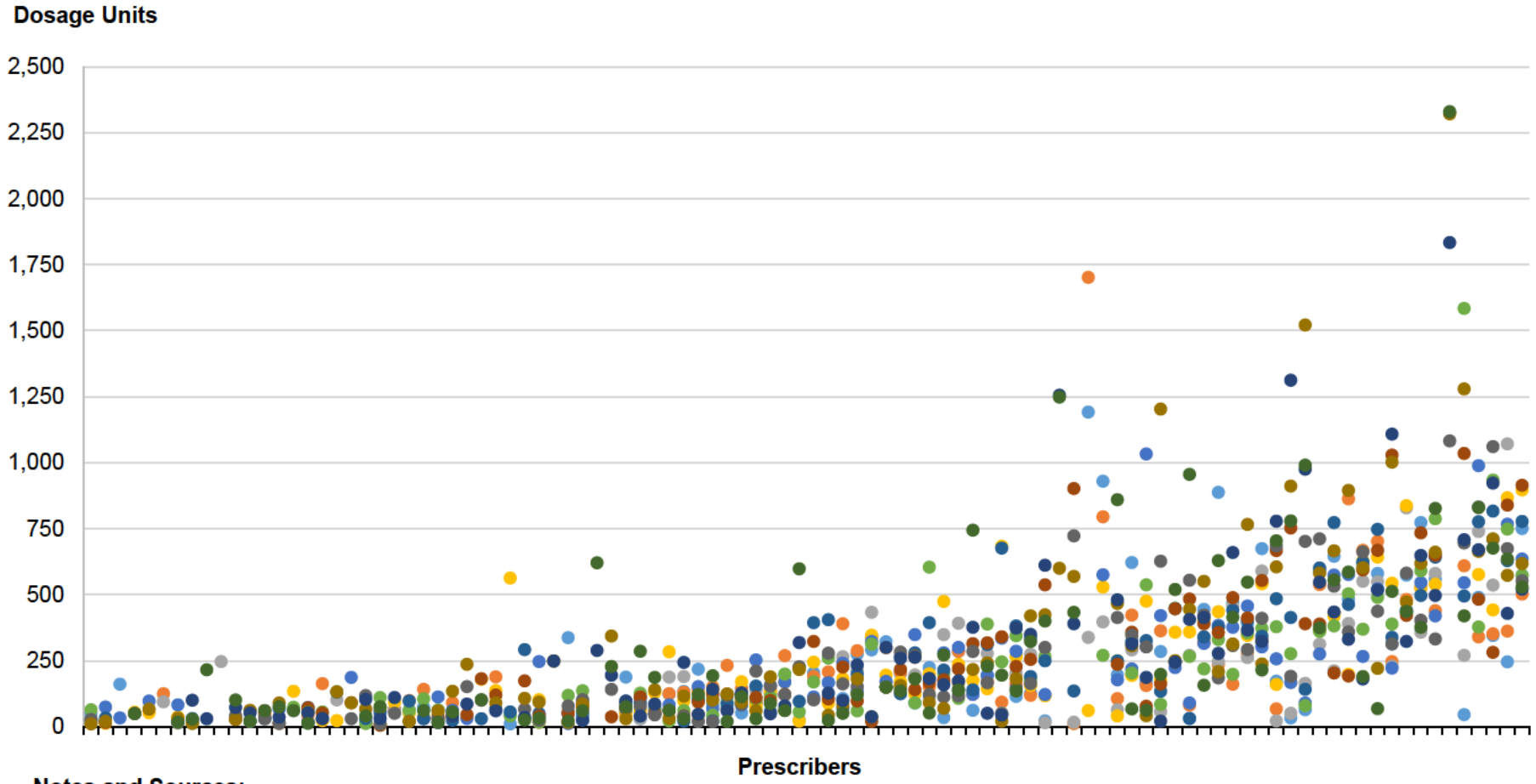
Monthly Prescribing of Oxycodone and Hydrocodone
Cuyahoga County, 2012



Notes and Sources:
IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622; see Data Appendix.
Sample is limited to a random sample of 100 prescribers for whom total prescribing in 2012 is in the interquartile range for Cuyahoga County.
Each marker corresponds to total dosage units written by a prescriber in a given month. Sample is limited to months with positive dosage units prescribed.

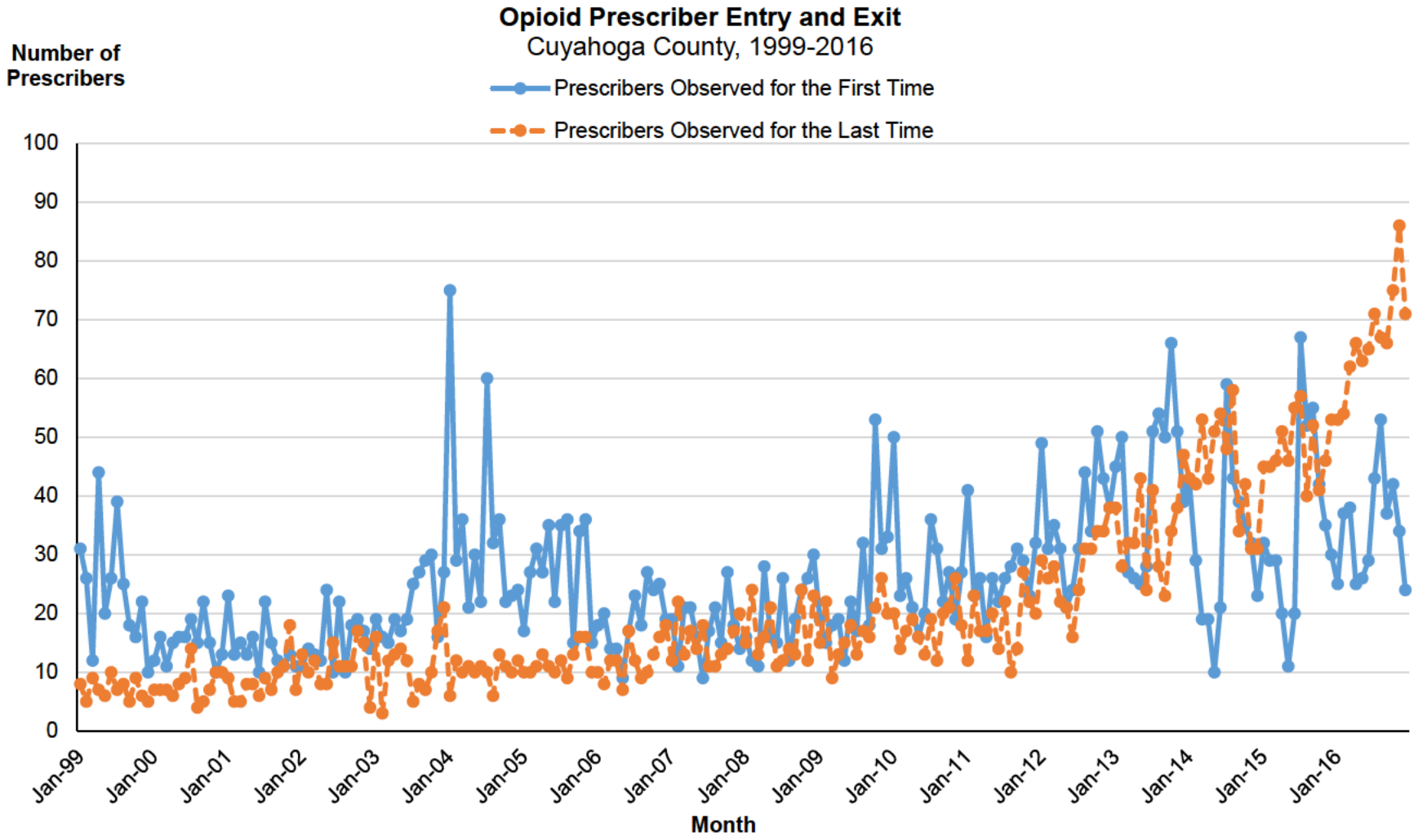
Exhibit VI-13

Monthly Prescribing of Oxycodone and Hydrocodone
Summit County, 2012



Notes and Sources:
IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622.
Sample is limited to a random sample of 100 prescribers for whom total prescribing in 2012 is in the interquartile range for Summit County. Each marker corresponds to total dosage units written by a prescriber in a given month. Sample is limited to months with positive dosage units prescribed.

Exhibit VI-14

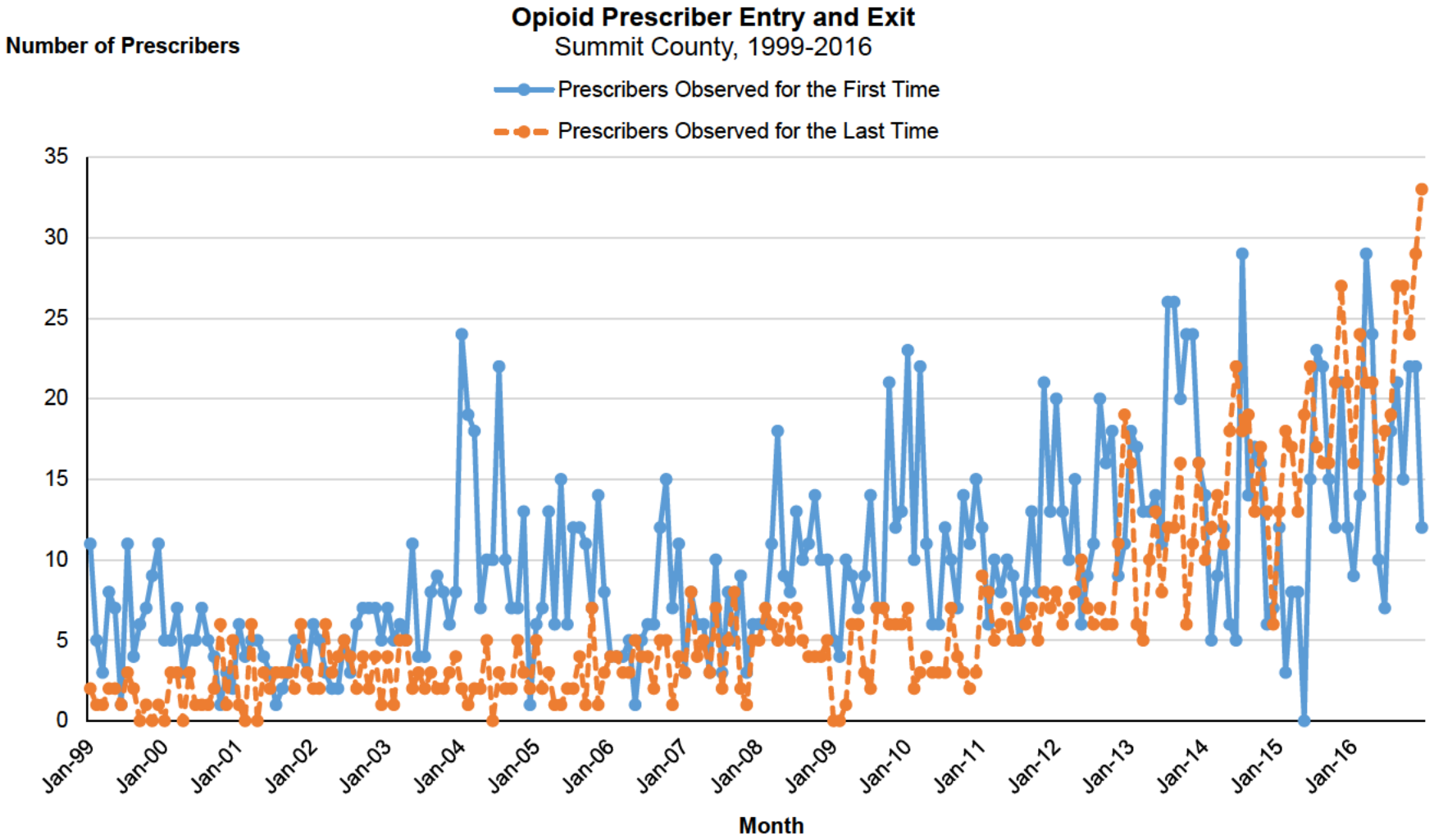


Notes and Sources:

IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622; see Data Appendix.

Sample is limited to prescribers located in Cuyahoga County with at least three months of positive prescribing in the data from 1997 and 2018. "Prescribers Observed for the First Time" is the number of these prescribers who first appear in a given month. "Prescribers Observed for the Last Time" is the number of these prescribers who last appear in a given month.

Exhibit VI-15



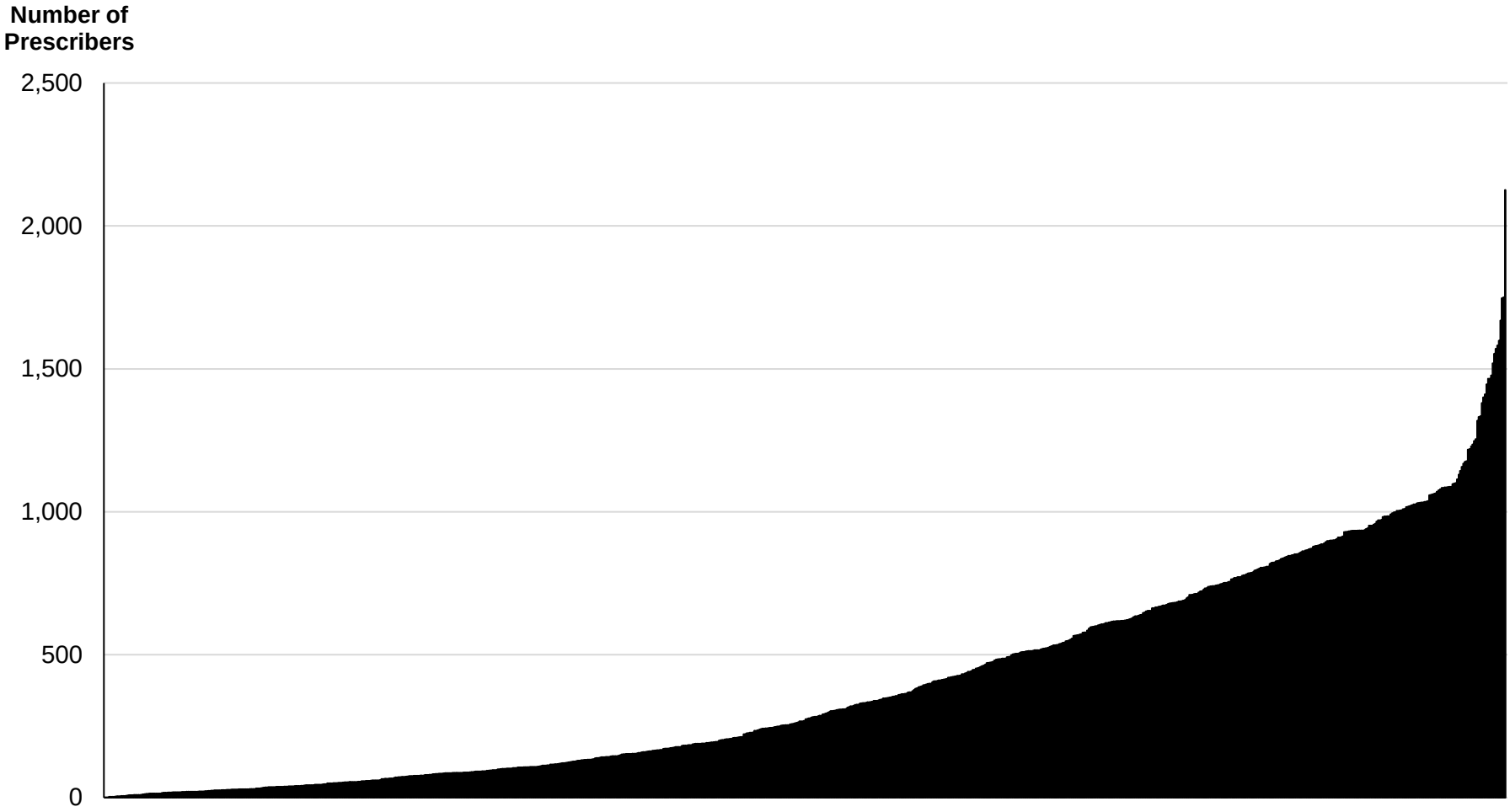
Notes and Sources:

IQVIA Xponent Data; "ZCTA to County Relationship File," United States Census Bureau, https://www.census.gov/geographies/reference-files/time-series/geo/relationship-files.html#par_textimage_674173622.

Sample is limited to prescribers located in Cuyahoga county with at least three months of positive prescribing in the data from 1997 and 2018. "Prescribers Observed for the First Time" is the number of these prescribers who first appear in a given month. "Prescribers Observed for the Last Time" is the number of these prescribers who last appear in a given month.

Exhibit VI-16

Distribution of Number of Prescribers with Opioid Prescriptions Filled at a Pharmacy
Cuyahoga and Summit Counties, 2012



Notes and Sources:
OARRS Data.
Sample is limited to prescriptions dispensed by pharmacies that reside in zip codes beginning in "44". Sample excludes pharmacies with fewer than 10 total filled prescriptions. Sample further excludes observations with negative patient age, non-positive days supply, negative authorized refills, and dosage units of a given prescription over 5,000.

Exhibit VI-17

Annual Number of Prescribers per Patient
Cuyahoga and Summit Counties, 2008-2017

Number of Patients

Number of Prescribers	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	436,321	471,181	466,751	475,105	482,365	434,337	428,192	433,415	408,373	374,681
2-4	169,415	182,482	189,572	195,127	199,726	187,201	188,134	185,120	167,488	139,670
5-9	14,933	15,777	18,321	18,360	17,083	19,510	20,818	19,304	16,017	10,879
10+	1,667	1,602	1,700	1,489	973	1,342	1,518	1,211	834	382
Total	622,336	671,042	676,344	690,081	700,147	642,390	638,662	639,050	592,712	525,612

Percent of Patients

Number of Prescribers	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	70.1%	70.2%	69.0%	68.8%	68.9%	67.6%	67.0%	67.8%	68.9%	71.3%
2-4	27.2%	27.2%	28.0%	28.3%	28.5%	29.1%	29.5%	29.0%	28.3%	26.6%
5-9	2.4%	2.4%	2.7%	2.7%	2.4%	3.0%	3.3%	3.0%	2.7%	2.1%
10+	0.3%	0.2%	0.3%	0.2%	0.1%	0.2%	0.2%	0.2%	0.1%	0.1%
Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

Dosage Units (Millions)

Number of Prescribers	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	55.3	60.2	59.8	64.5	66.4	59.3	54.4	51.3	49.8	44.0
2-4	68.2	73.8	80.9	82.0	83.0	82.0	78.2	73.8	67.6	56.2
5-9	15.5	15.2	18.6	17.5	15.3	19.4	19.7	16.8	13.7	9.3
10+	2.5	1.9	2.4	1.9	1.1	1.7	1.7	1.2	0.8	0.4
Total	**141.6**	**151.2**	**161.7**	**165.9**	**165.9**	**162.4**	**153.9**	**143.1**	**131.9**	**109.9**

Percent of Dosage Units

Number of Prescribers	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	39.1%	39.8%	37.0%	38.9%	40.1%	36.5%	35.3%	35.9%	37.8%	40.0%
2-4	48.2%	48.8%	50.0%	49.4%	50.1%	50.5%	50.8%	51.6%	51.2%	51.2%
5-9	11.0%	10.1%	11.5%	10.6%	9.2%	11.9%	12.8%	11.7%	10.4%	8.4%
10+	1.8%	1.3%	1.5%	1.1%	0.7%	1.0%	1.1%	0.9%	0.6%	0.4%
Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

Notes and Sources:
OARRS Data.
Sample is limited to patients aged 15 and over and excludes prescriptions for buprenorphine, naloxone, and any NDC code for which no MME conversion was available. Sample further excludes prescriptions with non-positive days of supply; prescriptions with a missing or non-positive quantity, or a quantity greater than 5000; prescriptions with missing prescriber ID; and prescriptions with a negative number of refill. "Number of Prescribers" indicates the number of unique prescribers for which an opioid prescription was obtained over the course of the calendar year.

Exhibit VI-18

Annual Number of Pharmacies Filling Prescriptions per Patient

Cuyahoga and Summit Counties, 2008-2017

Number of Patients

Number of Pharmacies	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	497,668	536,237	541,002	552,363	557,910	502,015	498,493	508,519	479,016	439,271
2-4	116,181	126,070	126,425	129,438	135,450	132,132	132,609	124,366	109,125	83,867
5-9	7,744	8,100	8,361	7,833	6,567	7,909	7,295	5,979	4,479	2,440
10+	743	635	556	447	220	334	265	186	117	34
Total	622,336	671,042	676,344	690,081	700,147	642,390	638,662	639,050	592,737	525,612

Percent of Patients

Number of Pharmacies	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	80.0%	79.9%	80.0%	80.0%	79.7%	78.1%	78.1%	79.6%	80.8%	83.6%
2-4	18.7%	18.8%	18.7%	18.8%	19.3%	20.6%	20.8%	19.5%	18.4%	16.0%
5-9	1.2%	1.2%	1.2%	1.1%	0.9%	1.2%	1.1%	0.9%	0.8%	0.5%
10+	0.1%	0.1%	0.1%	0.1%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

Dosage Units (Millions)

Number of Pharmacies	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	68.7	73.1	77.8	85.5	87.3	77.5	73.2	73.8	72.7	67.0
2-4	59.8	65.1	69.7	68.5	70.1	73.4	71.2	62.3	54.1	40.1
5-9	11.3	11.6	12.9	10.9	8.1	10.8	9.2	6.8	5.0	2.7
10+	1.8	1.4	1.3	1.0	0.4	0.7	0.4	0.3	0.2	0.1
Total	**141.6**	**151.2**	**161.7**	**165.9**	**165.9**	**162.4**	**153.9**	**143.1**	**131.9**	**109.9**

Percent of Dosage Units

Number of Pharmacies	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	48.5%	48.3%	48.1%	51.6%	52.6%	47.7%	47.5%	51.5%	55.1%	61.0%
2-4	42.2%	43.1%	43.1%	41.3%	42.3%	45.2%	46.2%	43.5%	41.0%	36.5%
5-9	8.0%	7.7%	8.0%	6.6%	4.9%	6.7%	6.0%	4.7%	3.8%	2.5%
10+	1.3%	0.9%	0.8%	0.6%	0.2%	0.4%	0.3%	0.2%	0.1%	0.0%
Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

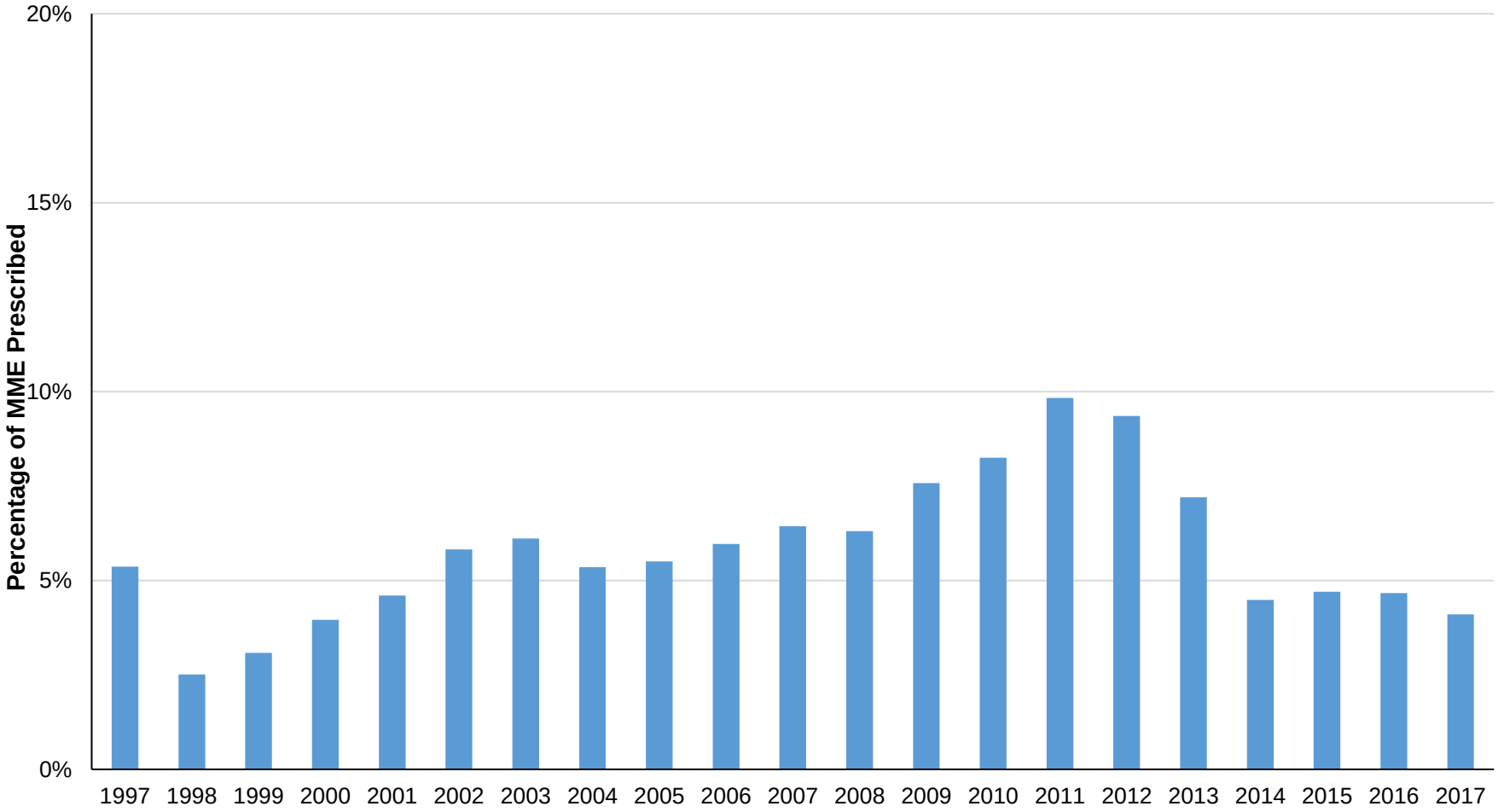
Notes and Sources:

OARRS Data.

Sample is limited to patients aged 15 and over and excludes prescriptions for buprenorphine, naloxone, and any NDC code for which no MME conversion was available. Sample further excludes prescriptions with non-positive days of supply; prescriptions with a missing or non-positive quantity, or a quantity greater than 5000; and prescriptions with a negative number of refill. "Number of Prescribers" indicates the number of unique prescribers for which an opioid prescription was obtained over the course of the calendar year.

Exhibit VI-19

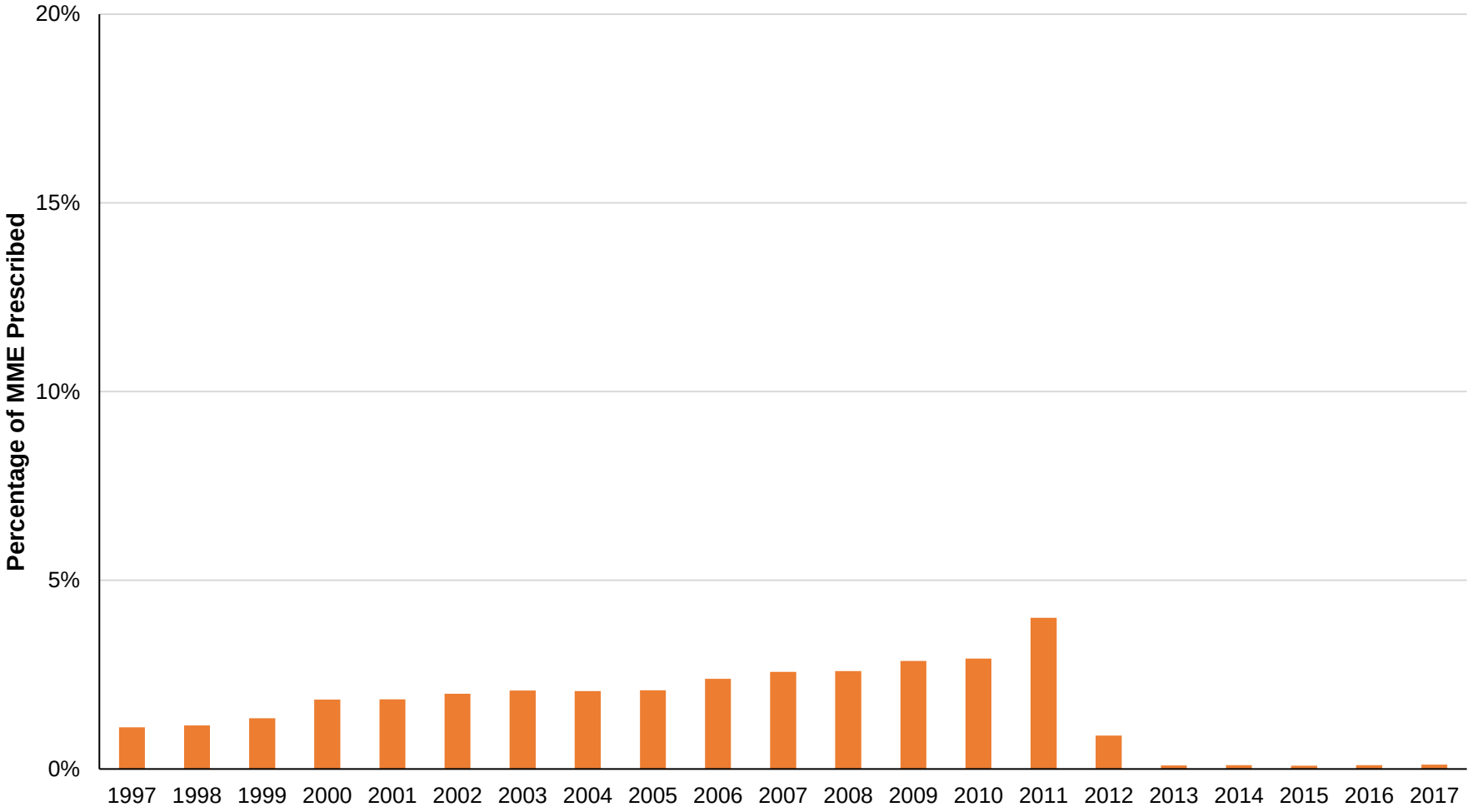
Percentage of Prescribing by Individuals Subject to Enforcement
Cuyahoga County, 1997-2017



Notes and Sources:
Appendix B (for identity of HCP subject to enforcement); IQVIA Xponent Data (for prescribing).

Exhibit VI-20

Percentage of Prescribing by Individuals Subject to Enforcement
Summit County, 1997-2017



Notes and Sources:
Appendix B (for identity of HCP subject to enforcement); IQVIA Xponent Data (for prescribing).

Exhibit VI-21

Potential Opioid Prescribing Arising Solely from Arthritis Pain, 2010

		MME	
		Cuyahoga	**Summit**
[1]	Number of adults	1,278,200	541,648
[2]	Percentage of adults with arthritis	28.5%	27.8%
[3]	Percentage of adults with arthritis who have severe joint pain	30.1%	30.1%
[4]	Percentage of regular opioids users	40%	40%
[5]	Daily dosage (MME/Day)	50	50
[6]	Duration (days)	365	365
[7]	**Potential opioid prescribing due to severe arthritis pain (MME)**	**800,447,825**	**330,865,356**

Notes and Sources:

[1] SEER Data.

[2-3] "State-Specific 2015 BRFSS Arthritis Prevalence Estimate statistics," CDC, https://www.cdc.gov/arthritis/data_statistics/state-data-current.htm#county. Severe joint pain prevalence is for Ohio.

[4-6] Expert Report of Edgar L. Ross, M.D., May 10, 2019, pp. 16-17.

[7] = product of [1] through [6].

Exhibit VI-22

Potential Opioid Prescribing Due Solely to Arthritis Compared to Actual Shipments, 2010

		MME	
		Cuyahoga	Summit
[1]	**Potential opioid prescribing due to arthritis pain**	**800,447,825**	**330,865,356**
	Opioid Shipments by Distributors		
[2]	ABDC	197,798,660	134,394,574
[3]	Cardinal	212,265,656	147,887,467
[4]	McKesson	122,790,413	105,644,481
[5]	Rite Aid	4,953,934	93,330
[6]	Walgreens	147,981,273	69,465,474
[7]	All Other Reporters	141,211,179	86,205,554

Notes and Sources:

[1] Exhibit VI-21 [7].

[2-7] ARCOS Data. Excludes buprenorphine.

Exhibit VII-1

Orders Reported to the DEA

2006 - 2014

[redacted]

Notes and Sources

ARCOS Data; confidential_suspicious_trans_oh_wv_al_il_mi_fl.xlsx and confidential_suspicious_trans_exclude_6states_20180529.xlsx.
Sample is limited to NDC codes found in the ARCOS Data and excludes buprenorphine. A "reported order month" is any calendar month with at least 1 order reported to the DEA.

Exhibit VII-2

Subsequent Ordering Following Reporting to the DEA

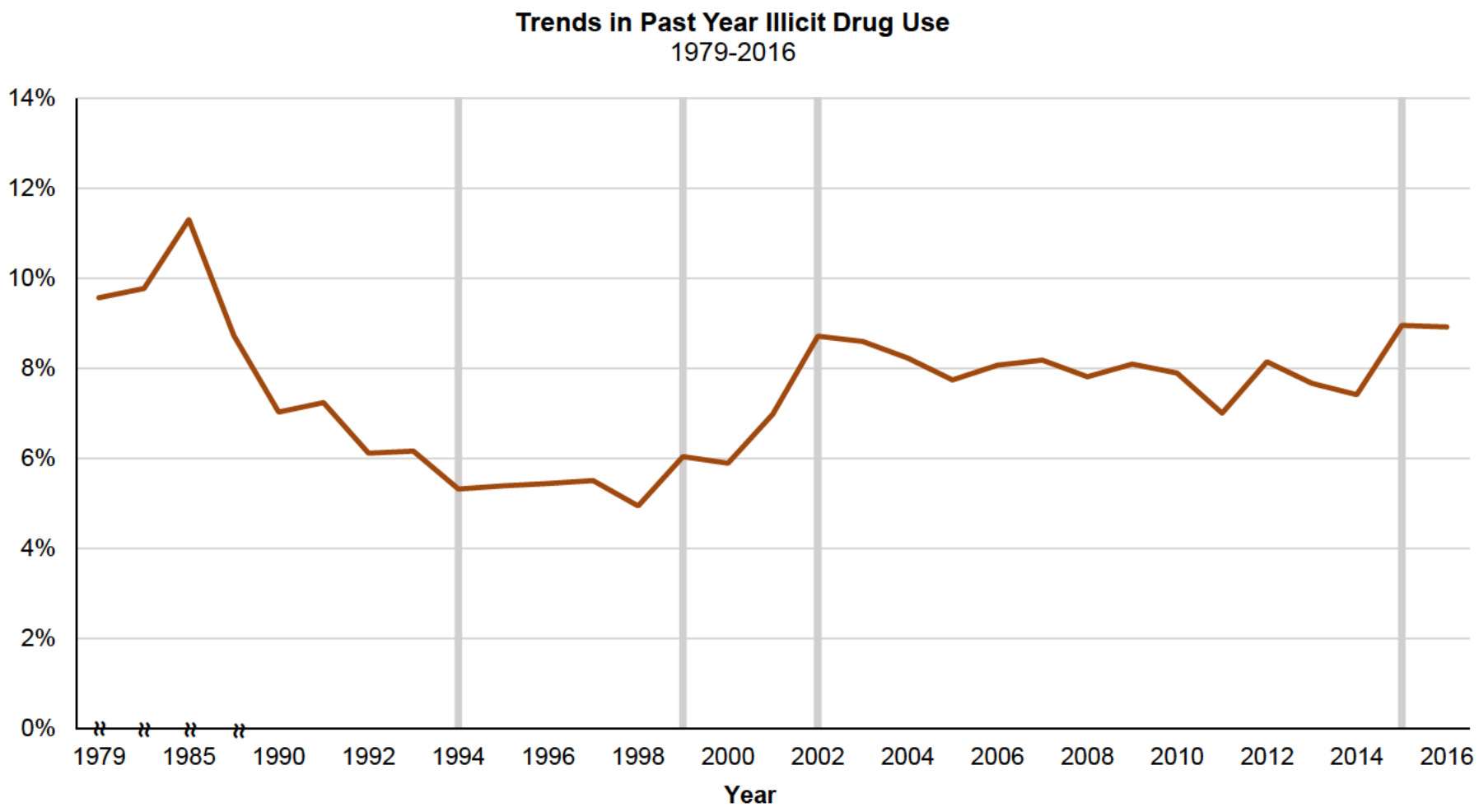
2006 - 2014

[redacted]

Notes and Sources:

ARCOS Data; confidential_suspicious_trans_oh_wv_al_il_mi_fl.xlsx and confidential_suspicious_trans_exclude_6states_20180529.xlsx.
Sample is limited to NDC codes found in the ARCOS Data. "Control Group" is constructed as follows: (i) For each pharmacy calculate a rolling 6-month average monthly shipments of MME; (ii) for each pharmacy whose last reported order is no later than June 1, 2014; define the month prior to the month of the first reported order as the "matching month"; (iii) find all pharmacies in the matching month with no observed reported order (up to December 31, 2014), of the same type, in the same county, and with a rolling 6-month average within 0.2 times and 5 times the rolling 6-month average of the target pharmacy; (iv) of these pharmacies choose the one whose rolling 6-month average is closest to that of the pharmacy in the month prior to its first reported order. Sample excludes pharmacies for whom no match was found.

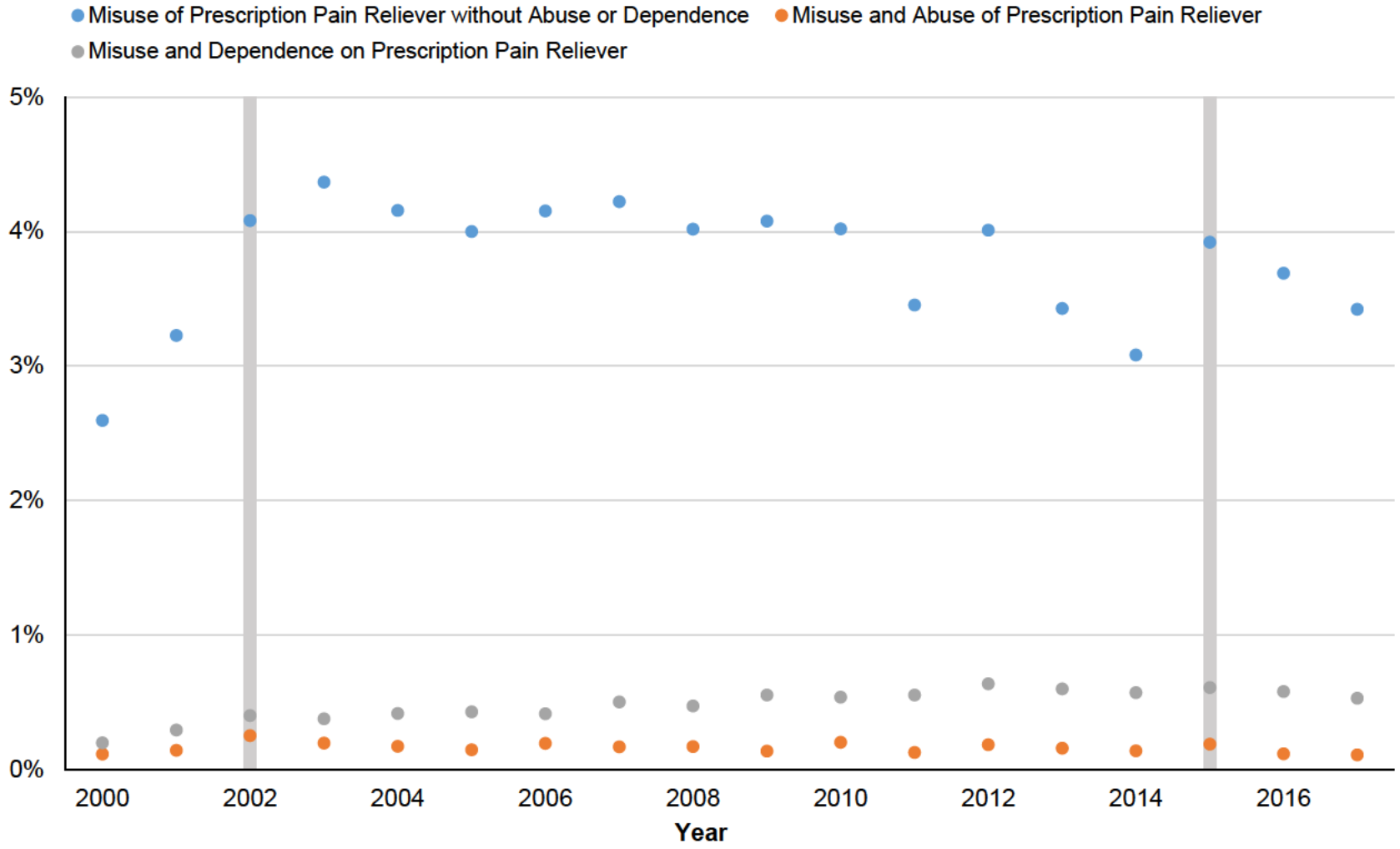
Exhibit VIII-1



Notes and Sources:
NSDUH Data.
"Illicit drug use" indicates use of heroin, hallucinogens, or cocaine (including crack), or the misuse of inhalants, tranquilizers, sedatives, stimulants, or prescription pain relievers.
Vertical bars represent relevant changes in NSDUH methodology or questions.
Break lines represent years in which the NSDUH survey was not conducted and no data are available.

Exhibit VIII-2

Trends in Prescription Pain Reliever Misuse, Abuse, and Dependence
2000-2017



Notes and Sources:
NSDUH Data.
Vertical bars represent relevant changes in NSDUH questions or methodology.

Exhibit VIII-3

Comparing Prescription Pain Reliever Misusers to Non-Misusers

	Past Year Prescription Pain Reliever Misuse (%)	No Past Year Prescription Pain Reliever Misuse or Heroin Use (%)	Differences	
			(1) - (2)	Statistically Significant? (P<0.05)
	(1)	(2)	(3)	(4)
Panel A: Demographics of Prescription Pain Reliever Misusers Compared to Non-Misusers				
Female	44.6	52.1	-7.5	Yes
White	72.3	68.1	4.3	Yes
Black	9.2	11.6	-2.5	Yes
Hispanic	13.6	13.7	-0.1	No
Age 18-25	26.5	10.5	16.0	Yes
Age 26-34	18.4	11.8	6.7	Yes
Age 35-64	28.2	40.4	-12.2	Yes
Age 65+	2.0	13.6	-11.6	Yes
High School Dropout	18.3	15.0	3.3	Yes
Highest Education: High School	30.9	29.9	1.0	Yes
Highest Education: College	18.1	27.8	-9.7	Yes
Panel B: Drug Use of Prescription Pain Reliever Misusers Compared to Non-Misusers				
	Drug Use Prior to Prescription Pain Reliever Misuse (%)	**Lifetime Drug Use (%)**		
Cocaine	20.9	14.1	6.8	Yes
Hallucinogen	26.9	13.8	13.1	Yes
Heroin	1.9	1.3	0.6	Yes
Sedative	4.1	3.2	0.9	Yes
Stimulant	13.5	7.3	6.2	Yes
Any Illicit Drug Use[1]	45.2	25.0	20.2	Yes

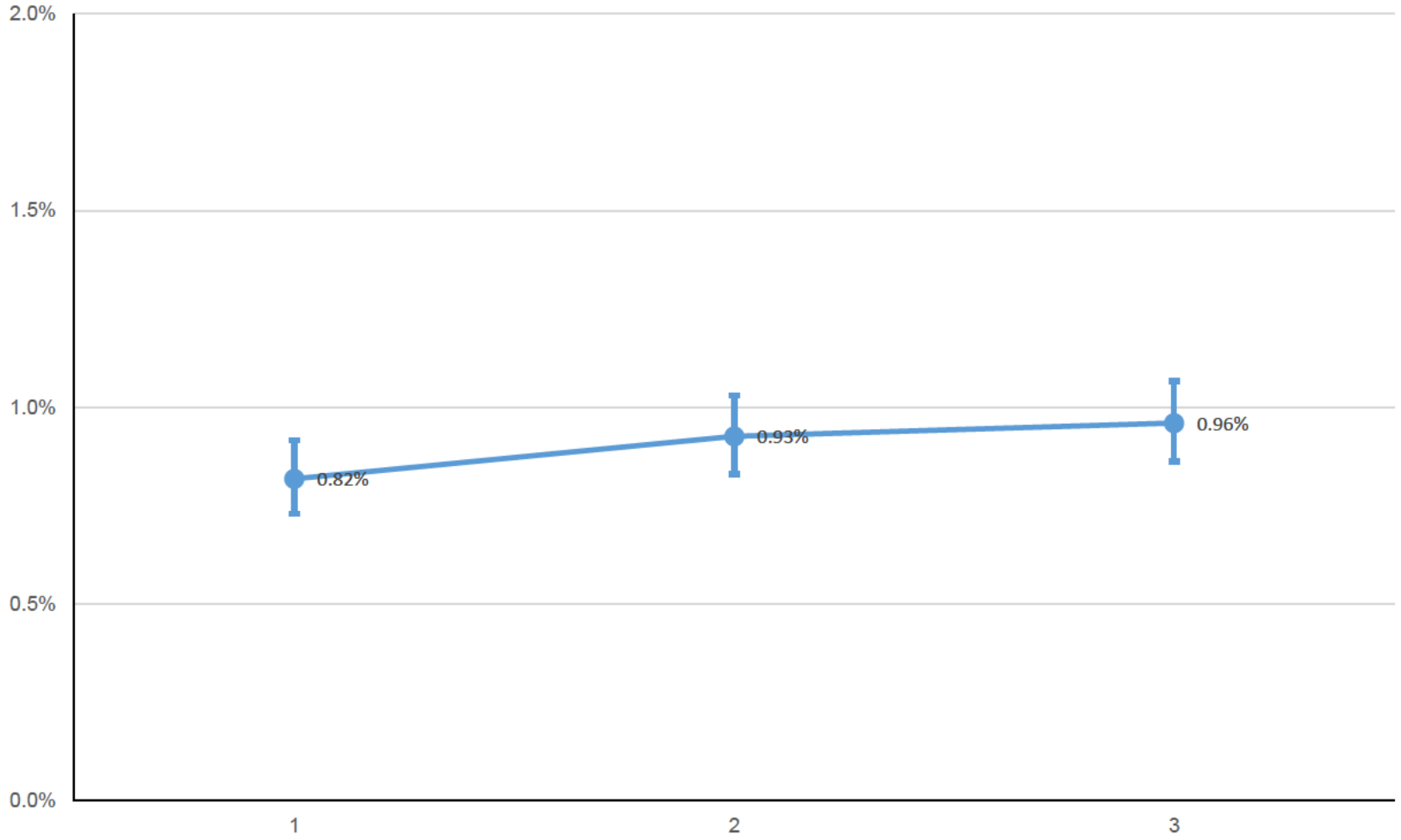
Notes and Sources:

NSDUH Data.

[1]"Illicit drug use" indicates use of heroin, hallucinogens, or cocaine (including crack), or the misuse of inhalants, tranquilizer, sedatives, or stimulants.

Exhibit VIII-4

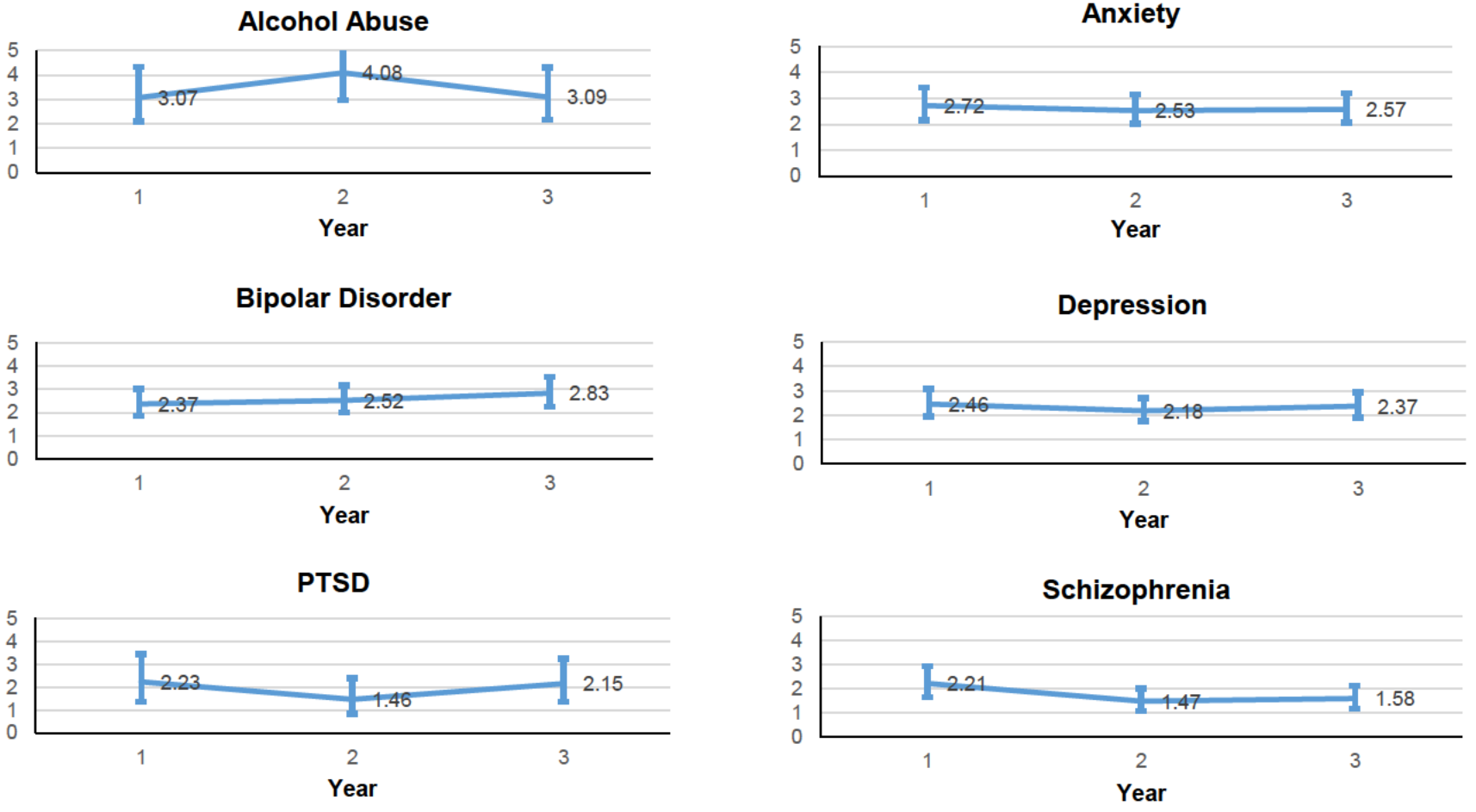
Annual Hazard Rate of Opioid Abuse / Dependence Diagnosis Following First Opioid Prescription



Notes and Sources:
Ohio Medicaid Data (2010 - Oct/2018).
Annual hazard rate of opioid abuse/dependence in a year is defined as the number of opioid users without an opioid abuse/dependence diagnosis at the end of the previous year who received an opioid abuse/dependence diagnosis during the year. The rate is calculated for opioid users >15 years old and enrolled 2 years before and 3 years after first opioid use. Bars represent 95% confidence intervals.

Exhibit VIII-5

Opioid Abuse / Dependence Odds Ratios for Certain Conditions Prior to First Opioid Prescription



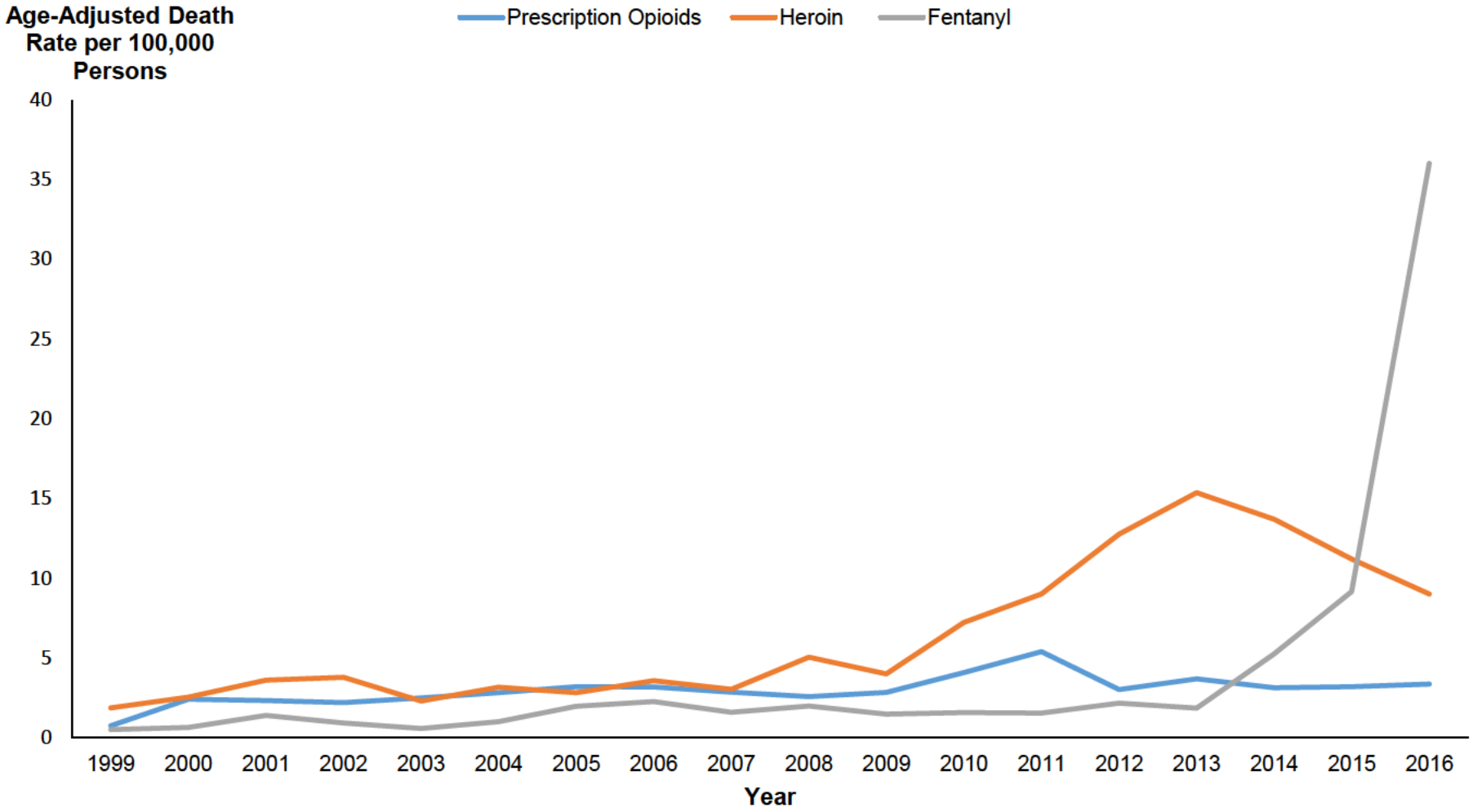
Notes and Sources:

Ohio Medicaid Data (2010 - Oct/2018).

Annual hazard rate of opioid abuse/dependence in a year is defined as the number of opioid users without an opioid abuse/dependence diagnosis at the end of the previous year who received an opioid abuse/dependence diagnosis during the year. The rate is calculated for opioid users >15 years old and enrolled 2 years before and 3 years after first opioid use. Odds ratio is calculated by comparing the rate for the group with the diagnosis versus the group without. Bars represent 95% confidence intervals.

Exhibit VIII-6

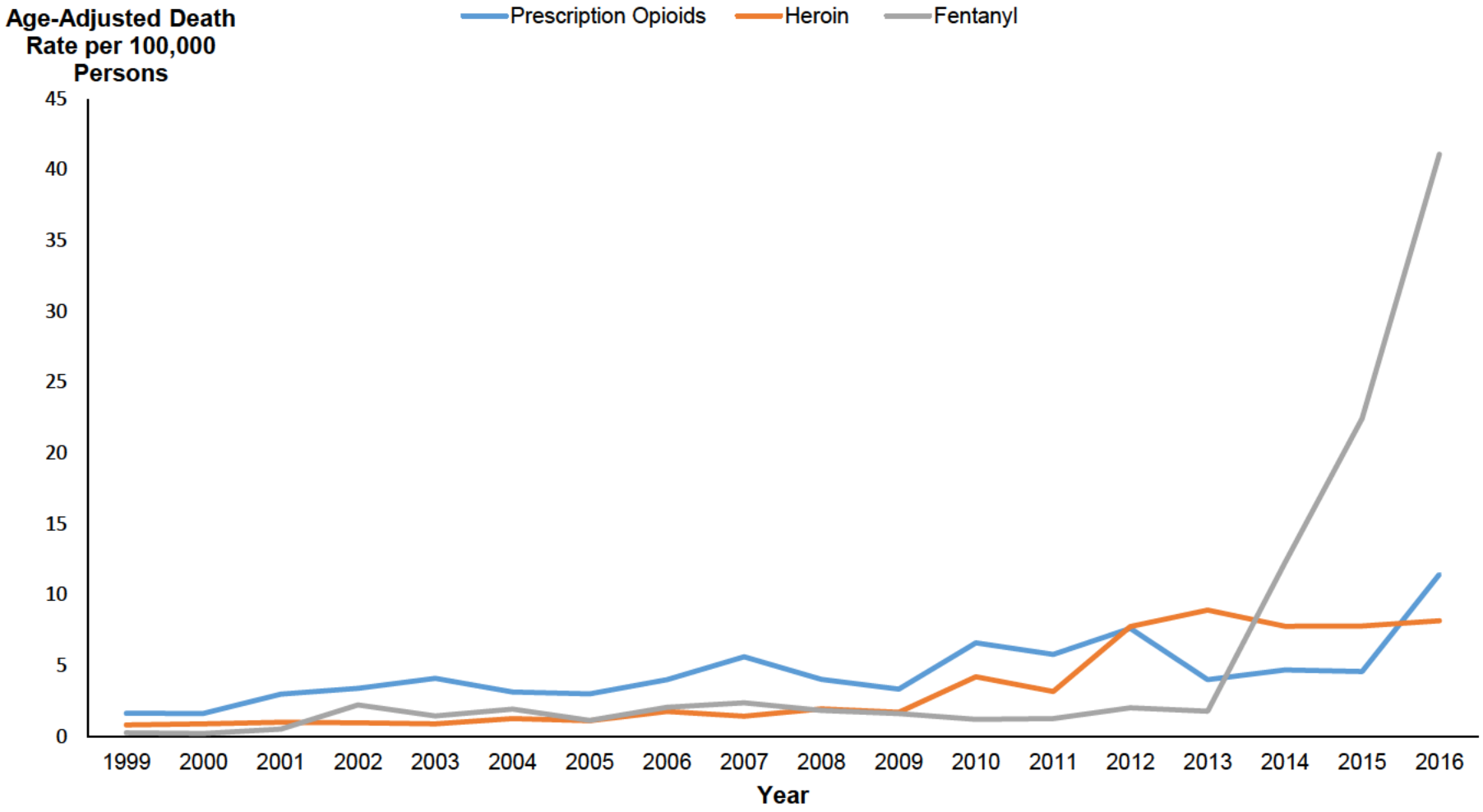
Opioid-Related Mortality Trends
Cuyahoga County, 1999-2016



Notes and Sources:
CDC Wonder. County FIPS codes are identified from the list published by United Sates Census ("Geographies," United States Census, https://www.census.gov/geographies/reference-files/2017/demo/popest/2017-fips.html). Data represent: prescription opioids (only); heroin (but not fentanyl); and fentanyl (with any additional opioids).

Exhibit VIII-7

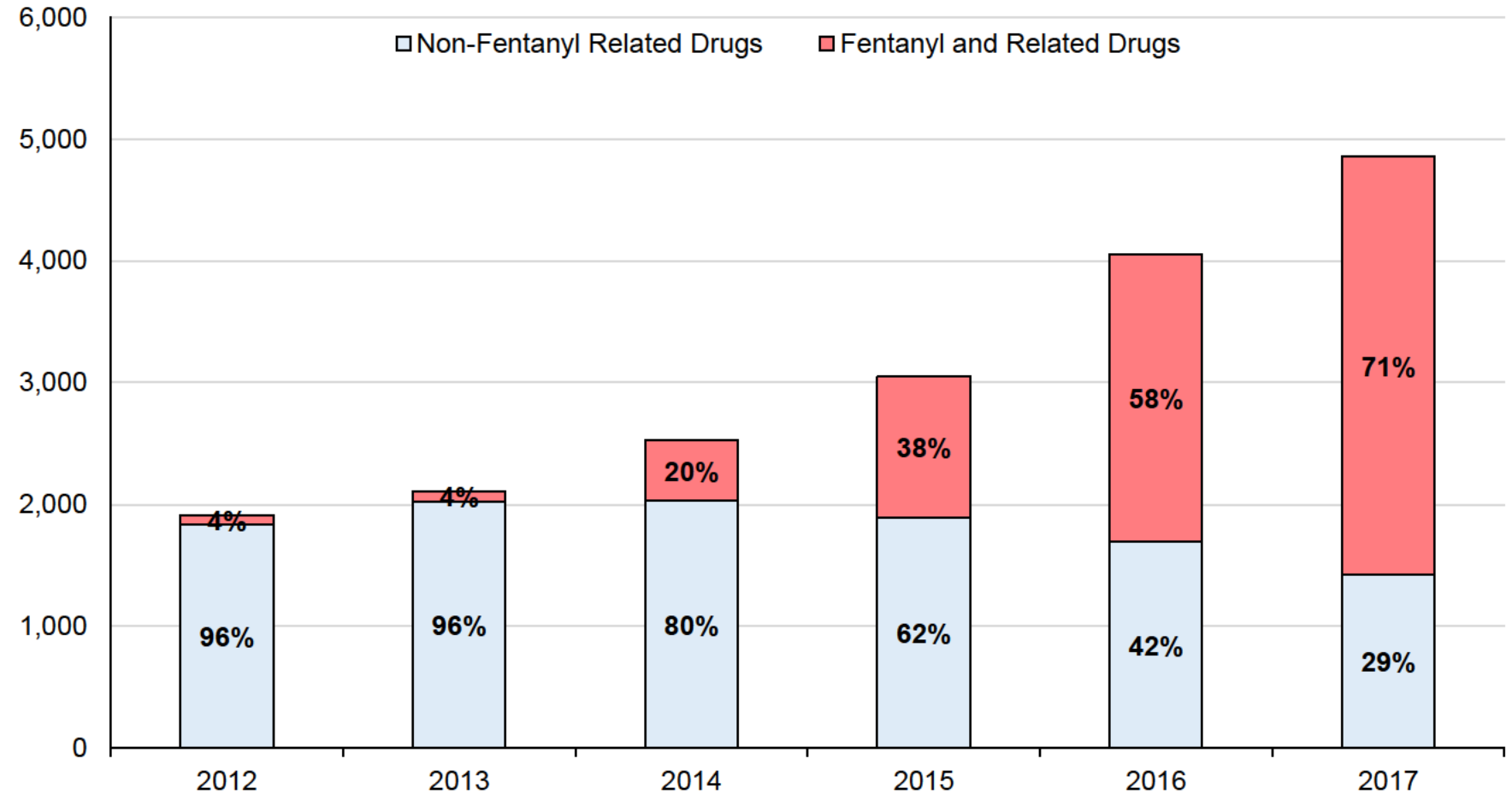
Opioid-Related Mortality Trends
Summit County, 1999-2016



Notes and Sources:
CDC Wonder. County FIPS codes are identified from the list published by United Sates Census ("Geographies," United States Census, https://www.census.gov/geographies/reference-files/2017/demo/popest/2017-fips.html). Data represent: prescription opioids (only); heroin (but not fentanyl); and fentanyl (with any additional opioids).

Exhibit VIII-8

Number and Share of Drug-Related Deaths due to Fentanyl and non-Fentanyl Related Products
Ohio; 2012-2017



Notes and Sources:
"2017 Ohio Drug Overdose Data: General Findings," Ohio Department of Health, 2018, Figure 7; "2017 Ohio Drug Overdose Data: General Findings," Ohio Department of Health, 2018, Figure 1.

Exhibit VIII-9

Comparing Prescription Pain Reliever Misusers based on Transition to Heroin Use

	Prescription Pain Reliever Misusers[1], who		Differences	
	Used Heroin in the Past Year (%)	No Heroin Use in Lifetime (%)	(1) - (2)	Statistically Significant? (P<0.05)
	(1)	(2)	(3)	(4)
Panel A: Demographics of Prescription Pain Reliever Misusers based on Transition to Heroin Use				
Female	27.3	45.3	-18.0	Yes
White	82.0	75.0	7.0	Yes
Black	5.9	8.5	-2.6	Yes
Hispanic	9.2	11.8	-2.6	Yes
Age 18-25	37.6	19.2	18.4	Yes
Age 26-34	26.8	18.8	8.0	Yes
Age 35-64	21.8	37.0	-15.2	Yes
Age 65+	0.4	2.5	-2.1	Yes
High School Dropout	26.0	14.4	11.7	Yes
Highest Education: High School	35.7	30.2	5.6	Yes
Highest Education: College	5.3	24.0	-18.7	Yes
Panel B: Prior Drug Use of Prescription Pain Reliever Misusers based on Transition to Heroin Use				
Cocaine	27.4	18.9	8.6	Yes
Hallucinogen	36.3	25.2	11.1	Yes
Sedative	5.6	4.6	1.0	No
Stimulant	16.3	12.7	3.6	Yes
Any Illicit Drug Use[2]	54.4	43.4	11.0	Yes

Notes and Sources:

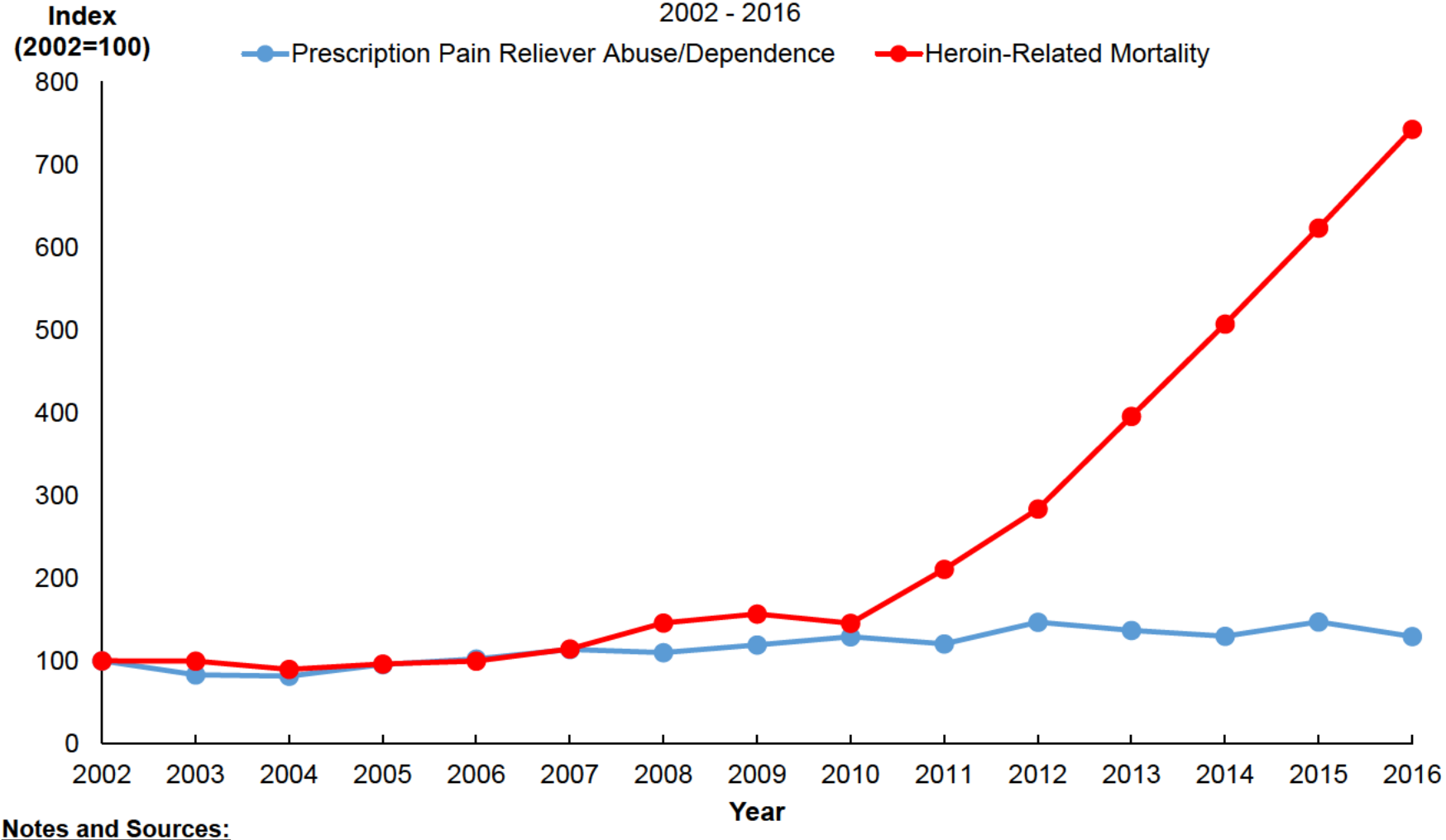
NSDUH Data.

[1] Sample based on prescription pain reliever misuse at any point in their lifetime and excludes prescription pain reliever misusers who used heroin prior to their prescription pain reliever misuse.

[2]"Illicit drug use" indicates use of hallucinogens, or cocaine (including crack), or the misuse of inhalants, tranquilizers, sedatives, or stimulants.

Exhibit VIII-10

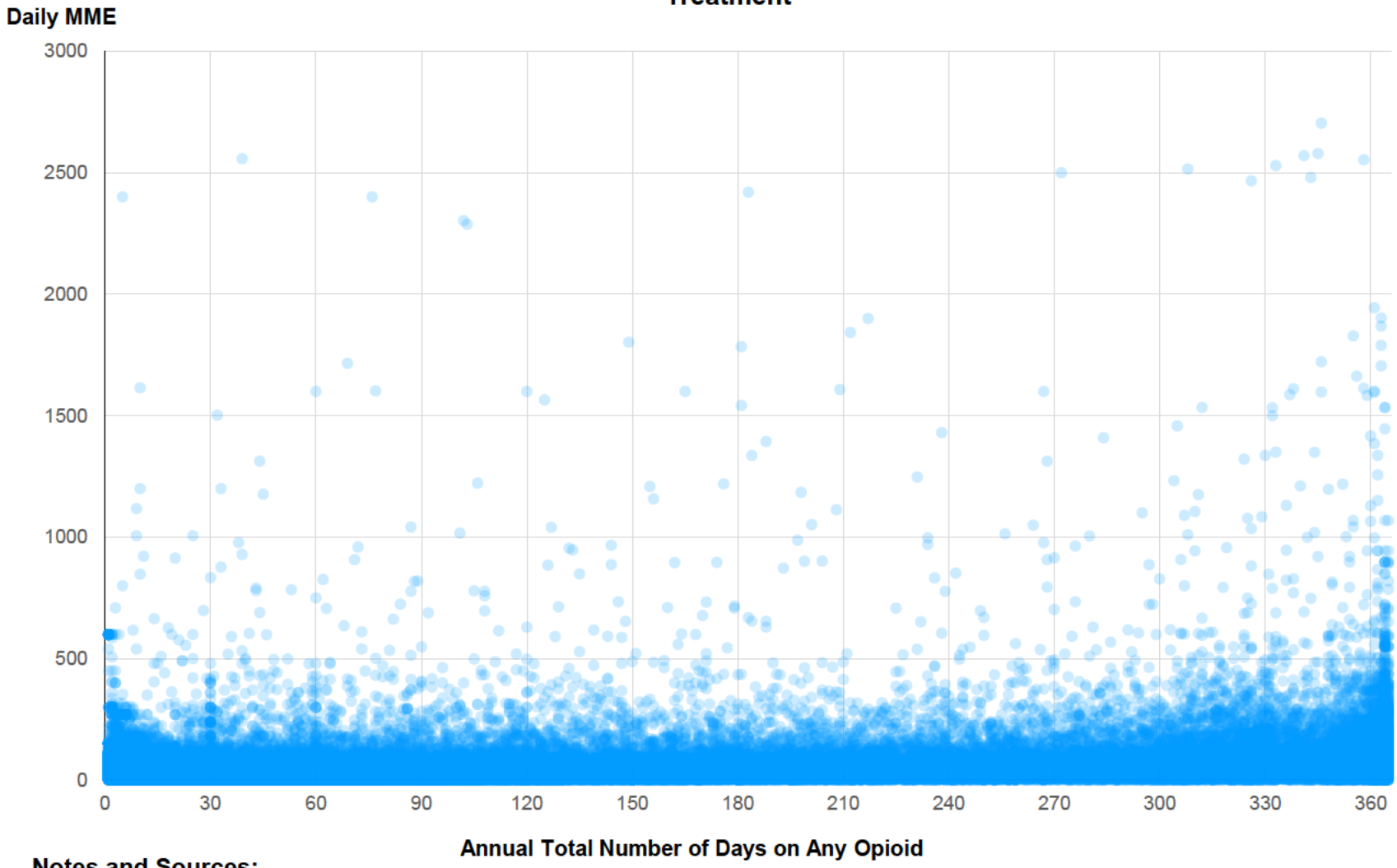
Change Over Time in Prescription Pain Reliever Abuse / Dependence and Heroin-Related Mortality
2002 - 2016



Notes and Sources:
NSDUH Data (for non-OTC pain reliever use disorder); CDC Wonder (heroin mortality).
"Opioid Abuse / Dependence" indicates NSDUH classification of prescription pain reliever abuse or dependence in the last year (see Appendix A) for further details; heroin-related mortality is defined as a drug-related death with ICD-10 code of T40.1 ("heroin"). Figures are not age or population adjusted. Sample is limited to ages 18 or older.

Exhibit VIII-11

Ohio Medicaid Beneficiaries: Daily Opioid MME and Annual Total Number of Days on Opioid Treatment



Notes and Sources:
Ohio Mediciad Data.
Includes all patients who have at least one opioid claim from 2010 to Oct/2018. Sample limited to patients >15 years old without any cancer diagnosis; each point represents a patient-year from Ohio Medicaid.

Exhibit VIII-12

Number of Ohio Medicaid Beneficiaries by Daily MME and Annual Total Number of Days on Opioid Treatment in 2017

	Days of Therapy in 2017							
Daily MME Range	<=30 days	31-60 days	61-90 days	91-180 days	181-270 days	271-360 days	361+ days	**Total**
(0, 30]	36,680	6,714	2,590	2,949	1,565	1,947	359	52,804
(30, 60]	12,920	731	365	671	525	1,023	361	16,596
(60, 90]	1,102	98	58	118	117	335	166	1,994
(90, 120]	228	22	11	35	52	109	55	512
(120, 150]	52	6	7	21	29	49	41	205
(150, 180]	11	4	6	10	15	28	24	98
>180	42	14	12	39	34	96	97	334
Total	51,035	7,589	3,049	3,843	2,337	3,587	1,103	72,543

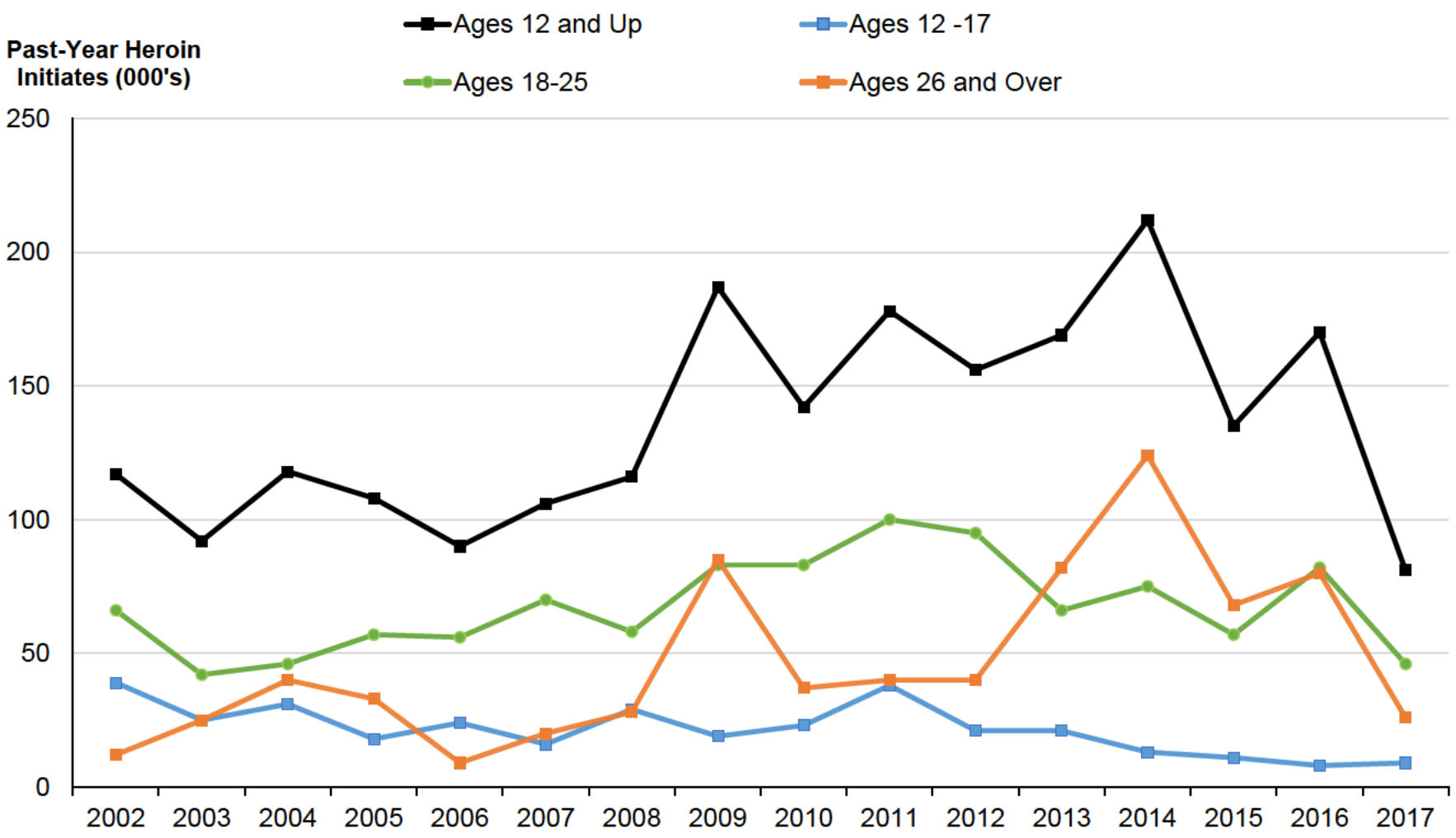
Notes and Sources:

Ohio Medicaid Data.

Sample limited to opioid patients > 15 years old and without any cancer diagnosis.

Exhibit X-1

Number of New Heroin Users
National, 2002-2017



Notes and Sources:
"Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health," HHS Publication No. SMA 18-5068, NSDUH Series H-53, Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, 2018, Figure 30.

Exhibit X-2

Ohio Medicaid Costs for Patients Diagnosed with Opioid Abuse / Dependence / Overdose

	Cost (1 Year Before)	Cost (1 Year After)	Cost Difference
1st Qu.	$1,964	$4,618	$-1,241
Median	$6,286	$11,075	$2,663
Mean	$17,028	$23,150	$6,122
3rd Qu.	$17,494	$25,432	$10,536

Notes and Sources:

Ohio Medicaid Data (2010 - Oct 2018).

Based on date of first opioid abuse / dependence / overdose diagnosis, for patients continuously enrolled for one year before and after; represents 23,382 patients.